

University of Nottingham

Gut Imaging for Function & Transit in Cystic Fibrosis Study 1

Study protocol 1 September 2018, NCT03566550

Brief Summary

Many people with Cystic Fibrosis (CF) are troubled by symptoms from their stomach and bowels: their gastrointestinal (GI) tract. Symptoms affect quality of life and can also reduce people's ability to digest enough calories to remain healthy, leaving them undernourished and less able to deal with other health problems such as infection.

Clinical tests to assess bowel function are limited. Many tests involve inserting a sensor or camera into the bowel, so they are not suitable for long periods, and can be uncomfortable. In Nottingham the investigators have developed imaging scans which can assess how someone's digestion works without any invasive device. The type of scanning the investigators use is called Magnetic Resonance Imaging, or MRI.

The purpose of this study is to see if those scanning methods can be used in people with CF to understand their digestion and any problems they have.

Detailed Description:

This is a small pilot study to establish that differences in digestion between people with and without CF can be quantified by repeated MR scans in fasted participants in response to standardised meals.

Participants will complete questionnaires on gastrointestinal function and symptoms: the PAC-SYM questionnaire, validated to assess symptom burden in adults with chronic constipation; and the CF abdomen questionnaire, developed in German for use in young people and adults with cystic fibrosis.

After this, participants only need to attend one study day at the Sir Peter Mansfield Imaging Centre. On this day they will be asked to withhold any medicines specifically targeted to alter bowel habit. This shall include laxatives but not enzyme

replacement therapy. They should attend on the study day having fasted since waking, other than water for essential medicines.

They will have their first MRI scan fasted. After the scan they will eat a standard test meal, and be scanned again first at half hour, then hour intervals until six hours after the first meal. The final scan will constitute the end of the study for each participant. Each session in the MRI scanner will last around 15 minutes. After each scan they will score their abdominal pain, bloating and flatulence symptoms on a Likert scale. In between scans, participants will have access to a lounge with wi-fi and a television.

Infection control requirements mean that the investigators are unable to scan more than one patient with CF on a single day. Patient scans will alternate with those of a Control participant. The investigators will aim to frequency match Controls with Patients for age and gender.

Study Design

Study Type: Observational

Actual Enrollment: 24 participants

Observational Model: Case-Control

Time Perspective: Cross-Sectional

Official Title: A Case-Control, Observational Study of the Postprandial Changes in Magnetic Resonance Imaging Parameters of Gastrointestinal Function and Transit in People With Cystic Fibrosis

Actual Study Start Date: September 4, 2018

Actual Primary Completion Date: February 20, 2019

Actual Study Completion Date: February 20, 2019

Group/Cohort	Intervention/treatment
CF people with cystic fibrosis	Diagnostic Test: MRI scans Repeated MRI scans imaging digestion of standard meals
Control people without cystic fibrosis	Diagnostic Test: MRI scans Repeated MRI scans imaging digestion of standard meals

Outcome Measures

Primary Outcome Measures:

1. oro-caecal transit time [Time Frame: 1 day of scanning] - time taken after eating for ingested food to be identifiable in the caecum on MRI

Secondary Outcome Measures:

1. gastric volume [Time Frame: 1 day of scanning] - volume of stomach at each time point of digestion to measure speed of gastric emptying
2. small bowel water content (corrected for body surface area) [Time Frame: 1 day of scanning] - volume of water content in small bowel representing secretions
3. colonic volume (corrected for body surface area) [Time Frame: 1 day of scanning] - volume of colon representing ease of chyme passage through colon

4. gastrointestinal symptoms [Time Frame: 1 day of scanning] - gastrointestinal symptoms as measured by questionnaires to monitor relationship with outcomes measured by MRI

Other Outcome Measures:

1. T1 relaxation time of ascending colon chyme [Time Frame: 1 day of scanning] - An approximate measure of water content in chyme present in the ascending colon
2. Fat fraction of the ascending colon chyme [Time Frame: 1 day of scanning] - A measure of fat content in chyme present in the ascending colon

Eligibility Criteria

Ages Eligible for Study: 12 Years to 40 Years (Child, Adult)

Sexes Eligible for Study: All

Accepts Healthy Volunteers: Yes

Sampling Method: Non-Probability Sample

Study Population

Nottingham and surrounding towns

Inclusion Criteria:

- Age 12 - 40 years
- Capacity to consent, or to understand the requirements of the study where parental consent is needed

PATIENTS: confirmed diagnosis of Cystic Fibrosis, either by sweat test or genetic testing; to reduce heterogeneity, we will only enrol homozygous CF patients with the most common CFTR mutation, p.Phe508del

CONTROLS: no clinical evidence or suspicion of Cystic Fibrosis

Exclusion Criteria:

Measurement of Forced Expiratory Volume in 1 second (FEV1) of <40% predicted using Global Lung Initiative criteria, according to clinical records

Contra-indication to MRI scanning, such as embedded metal, pacemaker

Unable to stop medications directly prescribed to alter bowel habit, such as laxatives or anti-diarrhoeals, on the study day

Previous resection of any part of the gastro-intestinal tract apart from appendicectomy or cholecystectomy. Surgical relief of distal intestinal obstruction syndrome or neonatal ileus will be permitted unless clinical records show excision of intestine >20cm in length.

Intestinal stoma

Diagnosis of inflammatory bowel disease or coeliac disease confirmed by biopsy

Gastrointestinal malignancy

Unable to comply with dietary restrictions required for the study

Statistical analysis plan

Data will be summarised through descriptive statistics. Differences between Patient and Control data will be tested using non-parametric methods. The software used will be GraphPad Prism version 7.0 or later, or SPSS version 21 or later, under licence to the University of Nottingham.

The primary and secondary outcomes will be compared firstly between CF patients and the non-CF controls using a t-test (for normally distributed variables) or a Mann-Whitney U test (for non-normally distributed data). We will then explore the association between the results of the symptom questionnaires and the MRI findings. We will compare MRI parameters such as OCTT, small bowel water and colonic volume against both the total CF Abdomen-Score and against the score for individual domains. An example of the latter would be comparing OCTT with the domains of “constipation” & “too much time spent on the toilet” from the CF Abdomen-score. We will compare these using a t-test or Mann Whitney U test, where the MRI parameter is a binary or categorical variable, and Pearson or Spearman’s correlation coefficient for continuous MRI parameters.

Where data is missing, through participant withdrawal or technical failure (e.g. scanner breakdown), an imputed value will be assigned which will be the median value for that parameter of other participants in the participant group (Patient/Control) at that time point.