Assessment of Colonic Epithelial Integrity with Mucosal Impedance

NCT Number: NCT03165058

Document Date: August 8th, 2016

Assessment of Colonic Epithelial Integrity with Mucosal Impedance

PI: Yash Choksi, MD
Vanderbilt University Medical Center
Gastroenterology, Hepatology, and Nutrition

Table of Contents:

Background:

Inflammatory Bowel Disease (IBD) is a chronic, incurable disease, and its pathogenesis is incompletely understood. Over one million individuals in the United States, over 200,000 Canadians, and over 2.5 million Europeans are estimated to have IBD. In the US, the direct medical cost is estimated to be over 6 billion dollars.

One of the challenges in the management of IBD patients is determining endpoints for treatment so as to prevent relapse of disease. Whether to treat patients with a goal of clinical remission (the patient's symptoms have improved), endoscopic remission (normal appearance of the mucosa during endoscopy), or histologic remission (normal appearance of biopsied tissue) can be a difficult decision since the medications (i.e. anti-TNF, immunomodulators) used in treatment of IBD all have significant side effects. This clinical scenario is common and is a reflection of our lack of understanding of the disease process.

Barrier function is suspected to play a role in the pathogenesis of IBD and at this time there is no convenient way to measure this *in vivo*. The overall goal of this project is, therefore, to develop a novel, minimally invasive technology to detect mucosal damage based on mucosal conductivity changes in the colon and use those measurements as an approximation of barrier function. We predict that these measurements will be helpful in predicting relapse in IBD and also serve as a clinical endpoint in treatment of IBD.

Rationale and Aims:

The intestinal epithelium functions to separate luminal contents from the interstitium. Increased intestinal permeability can represent compromise of the epithelium's integrity. Prior research has demonstrated that defects in intestinal barrier function are associated with inflammatory bowel disease (IBD) and increased intestinal permeability can be important in the maintenance of remission in IBD patients.

There is currently not a convenient way to measure colonic epithelial barrier function in real time. The lactulose/mannitol ratio measures small intestinal permeability but both are degraded by colonic bacteria and thus do not measure colonic permeability. Confocal endomicroscopy of images taken during colonoscopy (also of the small intestine - specifically of the terminal ileum) using a special endomicroscope colonoscope has also been shown to predict relapse in IBD patients. Imaging, however, required injection of a permeability probe during the procedure and then after the procedure the images needed to be analyzed by an expert.

In this study, we propose to use a novel, minimally invasive technology to detect mucosal damage (i.e. barrier dysfunction) based on mucosal conductivity changes in

the colonic epithelium. This mucosal impedance (MI) test was developed from collaborative work with Sandhill Scientific, Inc. and is already being implemented at Vanderbilt University for the assessment of esophageal epithelial integrity.

Our hope is that a greater understanding of barrier function, via measurement of MI, in the colon of IBD patients can provide clinically relevant information to help make these difficult decisions easier.

Previous Human Studies:

There have been no previous human studies using this device in the colon.

There have, however, been trials using it in the esophagus. One example is IRB #120126.

Inclusion/Exclusion:

This study will be inclusive of all adults who meet the inclusion/exclusion criteria and who are at least 18 years of age through age 99. In order to meet our objectives, we anticipate that up to 60 people will be enrolled.

Inclusion criteria:

A. Men and women over the age of 18 with a diagnosis of IBD (Ulcerative Colitis or Crohn's disease).
B. Men and women undergoing screening colonoscopy (typically age would be 50 or greater but there are exceptions)

Exclusion criteria

A. Age < 18 years old
B. Patient unable to give informed consent
C. Patients with history of colonic surgeries
D. Patients with history of colonic motility disorder

Enrollment/Randomization:

Patients will be identified by either Dr. Vaezi or Dr. Schwartz. Those patients undergoing colonoscopy for either the indication of screening colonoscopy or IBD surveillance will be asked, on the day of their colonoscopy, whether they want to participate in the study. They will then be consented for the procedure. There will not be randomization.

All subjects must sign an informed consent form that complies with the requirements of both 21 CFR Part 50 and Health Insurance Portability and Accountability Act (HIPAA) before entering the trial. An IRB-approved consent form that complies with the requirements of 21 CFR Part 50, including a HIPAA compliant authorization form for the use and disclosure of the subject's protected health information, will be used.

Study Procedures:

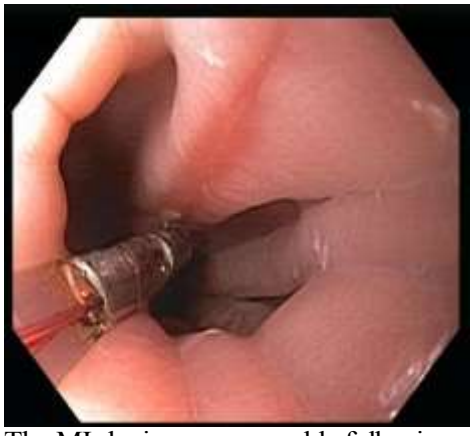
During routine colonoscopy, consented study participants will have a mucosal impedance catheter sensor positioned along the mucosal wall to measure resistance across the mucosa. The physician will take measurements in each segment of the colon, including segments that appear inflamed and normal adjacent areas (up to 10 locations). To obtain a stable reading, the sensor must remain in contact with the mucosa for five seconds. The catheter will be attached to a channeled feed that will record measurements on a dedicated computer using a software program designed by Sandhill Scientific, Inc. The study procedure will add approximately 1-2 minutes of anesthesia time for each participant.

This visit is the only required contact with the research volunteers. No further study procedures will be performed, and these subjects will not be contacted by research personnel following the visit.

Research material gathered from study participants will be limited to mucosal impedance data recorded during the routine colonoscopy. Basic demographic information, prior IBD treatments, and prior colonoscopic data will be collected from the electronic medical record following the procedure for those patients who consented to the research.

Device Description:

A single channel *MI* measuring rings separated by 0.2mm with a 360 degree circumferential design were mounted on a catheter, easily traversed through the working channel of an endoscope. The catheter tip has two 2 mm impedance sensors that are 3 mm apart which will make contact with the mucosa. The catheter tip will extend 5 cm from the scope end. The catheter body is manufactured from medical grade polyurethane which is routinely used in impedance-pH reflux monitoring catheters and is biocompatible.



The MI devices are reusable following proper cleaning technique. The probes are cleaned in the Digestive Diseases Motility Center with an enzyme solution (Aseptizyme) and then rinsed. They are placed into Cidex OPA for twelve minutes and then removed from Cidex OPA and rinsed with water. Cidex OPA is considered a high level disinfectant solution.

Potential Risks:

General Risks:
This study does not include interventions outside of what would be encountered for the standard care of these patients. The risk for participants in this study is theoretically low since the subjects are undergoing routine medical care (i.e. their colonoscopy is being done for other indications).

However, participation in the study will increase the amount of time that subjects are sedated by approximately 1-2 minutes. Increased exposure to anesthesia could potentially result in increased risk to the participant. This is outlined as below:
Common: Short-term memory loss that is usually brief, feeling drowsy, not being able to think clearly, decreased blood pressure and decreased respiratory activity (abnormal breathing);
Uncommon: Very low blood pressure, respiratory insufficiency (not breathing well enough to meet your body's needs), nausea and vomiting, abnormal heart rhythms, and a severe allergic reaction that could cause death;

Severe, Life-threatening and Rare: Breathing stops completely, the contents of the stomach get into the lungs, and low blood pressure that is severe enough to stop the heart.

Risks for Breach of Confidentiality:
There is a potential risk of breach of confidentiality associated with participation in any research study.

Minimizing Risks:
This study does not include interventions outside of what would be encountered for the standard care of these patients. Recruitment will be from patients who are seen

in the Digestive Diseases Center at Vanderbilt University Medical Center. Written informed consent will be obtained by research staff in accordance with the Vanderbilt Institutional Review Board policy and procedure.

The data will be stored in study specific binders in the GI Clinical Research Office. The GI Clinical Research Office is locked when not attended by study staff. Study documents will be kept indefinitely and stored in VUMC Storage and Services (VSS). The specimen reports also will be collected and kept in research file. The data will be coded and entered into a computer generated spreadsheet database. Patient confidentiality will be maintained in the computer database by not including any patient identifying information. The data will be coded by assigning each patient a number which is only accessible to study staff. Coded data will be shared with the biostatistician. Only the study staff will have access to participant names.

The PI meets with study staff weekly in order to monitor the progress of the study and study/participant issues. The PI will oversee all aspects of study conduct and is available to study staff via pager or cell phone.

The PI is responsible for data accuracy and protocol compliance. GI research staff will audit study records and monitor the data for accuracy.

Risk/Benefit Ratio:
No existing techniques can measure mucosal integrity in the colon in real time. This information may help direct management of IBD patients while increasing the risk of their procedure minimally by extending it by less than three minutes.

Adverse Event Reporting:
All serious and unanticipated adverse events or problems involving risks to subjects that may possibly be or are known to be related to the research activity will be reported promptly to the IRB office per Vanderbilt University IRB Policy. The PI will ensure proper data and safety monitoring for the materials and data used for the purposes of this study.

Study Withdrawal:
Patients may choose not to participate in this research study. This decision will not alter the routine care administered by the physician or the risks associated with standard of care procedures, i.e. colonoscopy. Additionally, the participant will be removed from this study if the investigator does not think it is in best interest for the patient to be in this study. If the patient is removed from the study he/she will be told the reason why.

Statistical Considerations:
No one has ever measured mucosal impedance in the colon and thus it is unknown whether there will be altered impedance in patients with active inflammatory bowel

disease versus normal tissue. Moreover, if there is a difference, it is not known how many patients will be required to show a statistically significant difference. Thus at this time, a power calculation cannot be done.

Privacy/Confidentiality Issues:
Subjects will have code numbers and will not be identified by name. Subject confidentiality is held strictly in trust by the participating investigators, their staff, the sponsor(s), and their agents. This confidentiality extends to the clinical information relating to participating subjects.

The study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party.

Confidentiality of subjects' records will be maintained; however, the Vanderbilt University Medical Center Institutional Review Board and applicable federal regulatory agencies may inspect the research records if needed. If any publications result from this study, only group or aggregate information will be published. Subject's name and identity will not be mentioned.

If subjects develop complications from endoscopy, the principal investigator will be readily available to assess the condition 24 hours a day and 7 days a week by phone or clinic visit or emergency room visit. The pager number, office number, hospital emergency room number will be given to the subjects when they are enrolled in the study.

Follow-up and Record Retention:
Follow-up is not required. The coded data collected for the purpose of this study will be maintained in a research database and will remain with Dr. Yash Choksi indefinitely.