Optimization of TEA Modalities for Treatment of IBS-C
NCT04953728
Date Approved: 4/21/2022

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: Optimization of TEA modalities for Treatment of IBS-C
Company or agency sponsoring the study: The Department of National Institutes of Health, Health and Human Services.
Principal Investigator: Jiande Chen Ph.D., Michigan Medicine, Department of Gastroenterology

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find child care, or make other plans. In your decision to participate in this study, consider all of these matters carefully.

This research is studying the use of a new device in 25 people to learn about its safety as an option for treating abdominal pain in patients with IBS-C. Rectal distension is the way the rectum is stretched when your body is ready to have a bowel movement. When your body experiences rectal distension, it sends a signal to your nervous system that you need to pass a bowel movement. Patients with IBS-C have difficulty recognizing this signal or feeling.

Past studies have demonstrated that acupuncture helps bring new awareness to patients with IBS-C by stimulating their nervous system and helping the body's signals work together. Transcutaneous Electrical Acustimulation (TEA) is similar to acupuncture but uses electric stimulation rather than the traditional needles. Researchers want to understand how TEA impacts your sensation of rectal distension.

This study has five visits detailed in section 4.1. Your health-related information in survey form will be collected for this research study.

This study involves a process called randomization. This means that the order of the TEA treatments that you receive in the study is not chosen by you or the researcher. - At one of your visits, a sham-TEA

(a placebo, or placement of a TEA patch without administration of a shock) will be performed instead of the actual TEA treatment. You will not be told at any visits if or whether you are receiving the TEA or the sham-TEA.

There can be risks associated with joining any research study. The risks of the study procedure may change whether you decide to join the study. For this study, although TEA is believed to be safe, some of these risks may include serious health complications of your current IBS-C such as bleeding and perforation. Perforation is a tear or hole in your rectum (please see section 5 for more information).

This study may offer some relief of your IBS discomfort. You may not gain any direct benefit by participating in this study.

You can decide not to be in this study. Alternatives to joining this study include seeking symptom relief alternatives from your gastroenterologist or joining other studies via the UM Health Research Portal.

Even if you decide to join the study now, you are free to leave at any time if you change your mind.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

Irritable bowel syndrome with constipation (IBS-C) is a common cause of chronic abdominal pain. This project is focused on the treatment of abdominal pain in IBS.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Inclusion criteria:
In order to be eligible to participate in this study, you must meet all of the following criteria:

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- You must be male or female and between the ages of 18 to 99
- You must be willing to comply with all study procedures and be available for the duration of the study
- You must be diagnosed with specific IBS-C satisfying Rome IV criteria
- You must have symptoms present for at least the last 3 months
- You must have abdominal pain that is not adequately relieved at the time of screening and the time of randomization
- You must have a VAS (Visual Analog Scale) pain score of >3 (on 0-10 score)
- Your abdominal pain is not adequately relieved at the time of screening.

Exclusion criteria:

- You have an unrelated active disorder which may involve abdominal pain, such as inflammatory bowel disease, diabetes, unstable thyroid disease
- You have history of abdominal surgery other than cholecystectomy (gallbladder removal) or appendectomy
- You are taking anticoagulants (medications which inhibit blood clotting) or antispasmodic (medications which inhibit involuntary muscle spasms), antidiarrheal, or opioids or other pain relief medications and cannot stop these medications for three consecutive days before each study visit.
- You are pregnant or breastfeeding.
- You have known allergic reactions to components of the ECG electrodes
- You received treatment with another investigational drug or other intervention within 6 months of the date of consent.
- Anything that, in the opinion of the investigator, would place the study participant at increased risk or preclude the study participant's full compliance with or completion of the study.
- You are unable to provide informed consent

3.2 How many people are expected to take part in this study?
25 subjects with IBS-C are expected to participate in this study.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?
You will have five research visits at the Gastrointestinal Physiology Lab at The University of Michigan. Each visit will be about the same. At each visit you will undergo a procedure called barostat test, which will be fully explained below.

Three days before each of your visits:
You will not take anticoagulants or antispasmodic, antidiarrheal, or opioids or other pain relief medications.

At 6:00pm before each of your visits:
You will fast (refrain from eating or drinking with the exception of unflavored water) before your visit. Please note: this includes coffee and tea.

During your visit:
You will go to the GI Physiology Laboratory within the Medical Procedures Unit. The research team will provide you with directions and a parking pass. For your privacy and comfort, you will be taken into one of the private GI physiology lab rooms.

If you are a woman of child bearing potential, you will be given a pregnancy test. If you are pregnant you cannot complete the study visit and will be withdrawn from the study.

You will be given a rectal enema. A rectal enema is a procedure in which liquid is injected into the rectum to clean the rectum.

You will complete a survey related to your IBS symptoms.

The GI Physiology Lab Staff will place electrocardiogram (ECG) electrodes on your skin. Electrodes are small metal discs that read electrical activity below your skin. Electrodes can also deliver electrical stimulation to your skin. Your skin will be cleaned using skin-prep materials before the electrodes are placed:

- 2 electrodes will be placed on your skin, either on one of your wrists or on one of your legs below your knee or. These two electrodes will be connected to the TEA device and deliver weak electrical current stimulation.
- 3 electrodes will be placed on your chest to record your cardiac activity.

A rubber (polyvinyl) catheter, called a barostat, will be placed 5-15 cm (1-6 in) into your rectum. A catheter is a thin tube. This tube is about the thickness of the cord used in corded headphones. The barostat will be inserted for 15 minutes at rest to collect baseline data.

The barostat has a small balloon at the end of the tube. The GI physiology lab staff will inflate a small balloon at the tip of the barostat to assess your ability to feel and recognize the sensation. This is to recreate the scenario of needing to pass a bowel movement. The rectum will stretch as your body experiences rectal distension.

During this period, you will be asked to take a note of your first sensation (the minimum level of inflation that you are aware of), urge to defecate (when you feel like you must go to the bathroom) and maximum tolerance (the highest level of sensation before it is painful).

Meanwhile, you will be asked to report the scale of pain or discomfort during the process of the balloon inflation.

Once your maximum tolerance is reached, the inflation will stop and the air will be removed. After this, one of the randomly assigned TEA methods (or sham-TEA) will be performed for 15 minutes. Then the inflation process described above will be repeated while applying the TEA.

At each visit you will have one of the five different TEA treatments. You may sense the weak electrical stimulation, and the stimulation intensity will be set a level you feel comfortable.

During the entire period, the ECG signal will be recorded from the three chest ECG electrodes.

4.2 How much of my time will be needed to take part in this study?

We expect each of the five visits to last about 120 minutes.

4.3 When will my participation in the study be over?
Your participation will conclude after you complete all five visits. The minimum time between two sessions is two days. The maximum time between sessions is four weeks.

4.4 What will happen with my information used in this study?
Your collected information may be shared with the Department of National Institutes of Health, Health and Human Services.

With appropriate permissions, your collected information may also be shared with other researchers, here, around the world, and with companies.

Your identifiable private information may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The immediate risks involved with barostat inflation to rectal distension include:
- Discomfort during the balloon insertion.
- Bleeding at the site of balloon inflation (in the rectum). The likelihood of this risk is rare, approximate incidence of <1%.
- Sensation (discomfort) with the balloon inflation which is a variable of the study. The likelihood of this risk is common, up to 100% of participants will experience discomfort. The study team will make the subject aware of this before they consent to the procedure. The subject has the right to stop the procedure at any time.
- However, the duration of rectal distention is brief and the distention can be immediately terminated upon intolerable pain or discomfort.

The long range risks of barostat inflation is:
- Perforation of the rectum into the peritoneal space, the likelihood of this risk is rare, approximate incidence of <1%.

The risks of electrical stimulation via TEA are:
- Possible allergic reaction to the stimulation electrodes and sensation of electrical stimulation. The likelihood of this risk is rare, approximate incidence of <1%
- However, the stimulation output will be set at a level that is well tolerated by the participant. In very rare occasions, the participant might experience rash or minor infection at the stimulation point that can be treated locally if needed.

The risk involved with the ECG recording:
- Allergic reaction of ECG electrodes. The likelihood of this risk is rare, approximate incidence of <1%.
- However, the risk will be minimized by screening against those with known electrode allergies.

The rationale behind these risks is that the risks are unlikely and the patient would receive care immediately. Moreover, the study team would not be able to collect this data without patients enduring the risks. Alternative procedures would not provide the same understanding of the influence of TEA for IBS-C patients.

The researchers will try to minimize these risks by having an experienced investigator and lab personnel performing the barostat studies with care. The study investigators and our GI Physiology lab staff have a lot of experience with these types of procedures. In addition, one of gastroenterologist-physician study investigators will be present or perform the studies or will be readily available on site for consultation or evaluation in case of any study complications or questions.

Additionally, there may be a risk of loss to confidentiality or privacy. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may experience some relief from your IBS-C discomfort from being in this study. A long-term possible benefit of the research could be that future patients with IBS-C have an alternative therapy for pain related to IBS-C. You may not gain any direct benefit by participating in this study.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?
Study participation is 100% voluntary. If you decide not to be in the study it will not impact your medical care.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information".

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
No harm would come to you if you decide to leave the study before it is finished.

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or cancelled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researcher's telephone number listed in Section 10.1.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
Subjects in this study will receive $200 per visit for visits 1-3 and $350 per visit for visits 4 and 5.

This totals to $1,300.00 once all study activity is completed.

8.3 Who could profit or financially benefit from the study results?
This study is completely supported and paid by the National Institutes of Health. Transtimulation research Inc. is working with the University of Michigan to develop the TEA device used in this study. If the study is completed successfully, the company may later try to gain FDA approval for the clinical use of the device. The study is designed by the investigators at The University of Michigan. The University may apply for patents and Transtimulation Research Inc. may license the patients from the University.

The company whose product is being studied:
Transtimulation Research Inc has made the device to be used in this study.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?
This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of child abuse and neglect, or harm to self or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

A description of this clinical trial will be available on http://www.clinicaltrials.gov/, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, Social Security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.
Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Jiande Chen Ph.D.
Mailing Address: Internal Medicine Gastroenterology
3912 TC
Ann Arbor, MI 48109-5362
Telephone: 734-647-9252

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies, include the appropriate calling codes.)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.
When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?
Your signature in the next section means that you have received a copy of this "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Consent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant with information about this study that I believe to be accurate and complete. The participant indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____