INDIANA UNIVERSITY INFORMED CONSENT STATEMENT FOR RESEARCH

High Resolution, Noninvasive Measurement and Functional Classification of Vagal Nerve Response Patterns in Relation to Gastroparesis Symptom Management using Gastric Electrical Stimulation Therapy

About this research
You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future. This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Taking part in this study is voluntary
You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with IU Health University Hospital.

WHY IS THIS STUDY BEING DONE?
You have been chosen to participate in this study because either you already have a Gastric Electrical Stimulation (GES) device implanted in your body for the treatment of your gastroparesis or are scheduled to have a new device placed by the surgeon or your device is not functioning properly and the surgeon is replacing the device or battery or wires. Gastroparesis is a condition that involves problems emptying the stomach. Some symptoms are vomiting, nausea, the feeling of being full right away when you start eating, and abdominal pain. Gastroparesis may also lead to malnutrition (a condition in which the body does not receive enough nutrients to properly function) and weight loss. Gastric electrical stimulation (GES) has been shown to be an effective treatment of nausea and vomiting in patients with gastroparesis. But, how GES works is unclear, as patients who undergo GES find that nausea and vomiting decrease before any improvement in gastric emptying is seen.

This study will be looking at the sensory nerve called the Vagus Nerve, and the Vagus nerve out flow, which is called vagal out flow. It has been suggested, but never proven, that GES may influence vagal outflow via vagal afferent fibers (fibers of the vagus nerve that carry sensation from the stomach to the brain) that carry sensory nerve impulses toward the Central Nervous System (CNS) (brain) where they terminate.

This study will help clarify if the improvement in the patients symptoms are related to the GES influencing the vagal outflow via vagal afferent fibers. This will help in finding the path of the vagus nerve in the neck and if the vagus nerve is affected by the gastric electrical stimulation. The vagus nerve wanders (follows a very unclear path which is why it is called vagus nerve) in the neck region and has different paths in different people. This study will try to find a common path for the vagus nerve.

This study is being conducted by Dr. Thomas Nowak, MD at the Indiana University School of Medicine. It is being funded by the National Institutes of Health (NIH).

HOW MANY PEOPLE WILL TAKE PART?
If you agree to participate, you will be one of 70 participants taking part in this research. There are 3 phases to the study: phase 1 will enroll 5-10 participants, and phase 2 will enroll 15-30 participants. You can enroll in either one, or both phases. Phase 2 will start only after all participants have been enrolled in

phase 1. Phase 3 involves all those who are either getting a new device or their device/ battery or wires are being replaced.

WHAT WILL HAPPEN DURING THE STUDY?
If you agree to be in the study, you will do the following things:

Phase 1:

1. You will sign this document, called an informed consent, that explains the study in detail and confirm that you agree to all the study procedures either in person or online virtually.
2. You will complete a symptom survey questionnaire and Gastric Cardinal Symptom Index (GCSI) questionnaire either in person or online.
3. Two electrocardiography (ECG) electrodes will be placed on both sides of your neck overlying the area near the carotid pulse (which overlies the carotid artery in the neck on the side of your neck) where the vagus nerve is located. This is done in order to measure the vagal nerve electrical impulses in the neck (electrical signal travelling in the nerve).
4. Two ECG electrodes will be placed on each of your arms or on the chest for measurement of electrocardiogram (ECG) (a test to measure the electrical activity of your heart)
5. Three ECG electrodes may be placed on your stomach to measure the electrical activity of the stomach.
6. After the placement of the electrodes, a 5-10 minute recording will be made.
7. Your GES device will be interrogated (data will be obtained) for the settings of your device and these will be recorded by the study team. After the 5-10 minute recording, the GES device will be turned off and another 2-4 minute recording will be made.
8. After the recording, the electrodes will be removed from your neck and a newer kind of electrodes called as MEA (Multi electrode Array)) devices that contain multiple (tens to thousands of small electrodes) will be placed on either one, or both sides of the neck. This film will help capture the vagus signal from a large area and help define the path of the vagus nerve.
9. After the placement of this film with small electrodes, another 5-10 minute recording will be made. The GES device will then be turned off and another 2-4 minute recording will be made.
10. With the GES device in the OFF mode, you may be asked to perform 2-3 procedures that stimulate the vagus nerve:
    a. Cold Stimulus: An ice cold wet towel will be placed on your face for approximately 10 seconds. This will be followed by 5-10 minute recording to look for any changes.
    b. Carotid Massage: A 10 second massage will be done over either the left or the right side of your neck. A 5-10 minute recording will be made after the massage.
    c. Valsalva maneuver: You will be asked to take a deep breath breathing in and blowing out into a mouthpiece that is hooked to a machine that measures how hard you are blowing. Alternatively, we can have you blow through the barrel of a 10 ml syringe for 15-20 seconds. After the 10 seconds of blowing out, a 5-10 minute recording will be made.
    d. Cough: you will be asked to cough for 10 seconds and a 5-10 minute recording will be made after you cough.
    e. The GES device will then be turned back on and the settings will be based on the initial settings you had before entering the study.
    Not all maneuvers will be done. You may be asked to perform 2-3 out of the 4 maneuvers.
11. The electrodes will then be removed and you will be allowed to go home.

The total time required for Phase 1 will be approximately an hour (60 minutes).

The first phase will help in better finding the right area where the MEA should be placed to get the best results.

The second phase will help in finding the exact path that the vagus nerve takes in each subject and the relation of the recording made through the MEA and the symptoms that you are experiencing for your gastroparesis and it will take place on a separate visit from Phase 1.

Phase 2:

1. You will sign this document, called an informed consent, that explains the study in detail and confirm that you agree to all the study procedures either in person or online virtually.
2. You will complete a symptom survey questionnaire and Gastric Cardinal Symptom Index (GCSI) questionnaire either in person or online.
3. Multiple electrodes (MEA) will be placed on either one or both sides of the neck.
4. One ECG electrodes will be placed on each of your arms or on the chest for measurement of electrocardiogram (ECG).
5. Three ECG electrodes will be placed on your stomach to measure the electrical activity of the stomach
6. After the placement of the electrodes a 5-10 minute recording will be made.
7. Your GES device will be interrogated (data will be obtained) for the settings and these will be recorded by the study team.

After this initial recording your stimulator will be reprogrammed to give 12 different combinations of settings and 2-3 minute recording at each setting will be made. Your stimulator will be programmed back to your original settings before you are sent home after the end of the study.

The settings to be used will cycle between several pulses with increasing amperage (how much energy is used to stimulate the nerve).

Another sequence that we can possibly use if we are unable to do the 12 settings sequence will be as follows. This will be used only if the investigator feels that the 12 settings sequence cannot be done.

8. .
   The GES stimulator will be reprogrammed to deliver the signal at 50% of the original power, and another 2-5 minute recording will be made.
9. Then, the device will again be programmed to deliver the signal at 25% of the original power setting on the device. Another 2-5 minute recording will be made.
10. After this, the device will be reprogrammed to the original settings.
11. The electrodes will then be removed and you will be allowed to go home.

The total time required for Phase 2 will be approximately an hour (60 minutes).

Phase 3:

1. You will sign this document, called an informed consent, that explains the study in detail and confirm that you agree to all the study procedures either in person or online virtually.
2. You will complete a symptom survey questionnaire and Gastric Cardinal Symptom Index (GCSI) questionnaire either in person or online

3. When the surgeon is either placing a new device or replacing a dead or malfunctioning device, battery, or wires, they will take photographs and video of the surgical procedure and the device placement.
4. This recording will then be de-identified (your name, date of birth and other information that can identify you) will be removed and the video will be then analyzed by the study team.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?
While participating in the study, the risks, side effects, and/or discomforts include:

There is a small chance of slight and temporary discomfort at the site where the electrodes are placed.

The main risks associated with the gel electrode array are local skin irritation due to the gel or to the adhesive, identical to those seen when using conventional single site electrodes. If any inflammation should occur during this study, it will be treated with topical antihistamines.

There is a risk of allergic reaction to medical adhesives, such as medical tape, and EKG lead placement adhesives. These reactions could include skin irritation, eruption, hives, or rash. On rare occasions, severe allergic reactions could include anaphylaxis (severe whole body allergic reaction).

Risk of using camera recording- the camera is built into the laparoscope and the surgeon's recording is within the clinical setting. It has minimal risk.

There also may be other side effects that we cannot predict.

There is a risk of potential loss of confidentiality.

WHAT ARE THE POTENTIAL BENEFITS OF TAKING PART IN THE STUDY?
We do not expect you to receive any benefit from taking part in this study, but we hope to learn things which will help scientists in the future.

WILL I RECEIVE MY RESULTS?
We may learn things about you from the study activities which could be important to your health or to your treatment. If this happens, this information will be provided to you. For example, we may find that you have an abnormal rhythm (arrhythmia) of your heartbeat. In that case, we will immediately inform you verbally of this abnormality and if indicated recommend further medical evaluation. You may need to meet with professionals with expertise to help you learn more about your research results. The study team/study will not cover the costs of any follow-up consultations or actions.

HOW WILL MY INFORMATION BE PROTECTED?
Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law. No information which could identify you will be shared in publications about this study

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the study investigator and his/her research associates, Purdue University, Axion Biosystems Inc., the Indiana University Institutional Review Board or its designees, and (as allowed by law) state or federal agencies, specifically the Office for Human Research Protections (OHRP), the Food

and Drug Administration (FDA) and the National Institutes of Health (NIH), who may need to access your medical and/or research records.

A description of this clinical trial will be available on ClinicalTrials.gov as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

For the protection of your privacy, this research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers may not disclose or use any information, documents, or specimens that could identify you in any civil, criminal, administrative, legislative, or other legal proceeding, unless you consent to it. Information, documents, or specimens protected by this Certificate may be disclosed to someone who is not connected with the research:

(1) if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases);
(2) if you consent to the disclosure, including for your medical treatment;
(3) if it is used for other scientific research in a way that is allowed by the federal regulations that protect research subjects;
(4) for the purpose of auditing or program evaluation by the government or funding agency;
(5) if required by the federal Food and Drug Administration (FDA).

A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself. 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.

WILL MY INFORMATION BE USED FOR RESEARCH IN THE FUTURE?
Information from this study may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information is shared. Since identifying information will be removed, we will not ask for your additional consent.

WILL I BE PAID FOR PARTICIPATION?
You will be paid $50 in gift cards for participating in the Phase 1 part of the study. You will be paid $50 in gift cards for participating in the Phase 2 part of the study. You will be paid $25 for Phase 3 part of the study.

WILL IT COST ME ANYTHING TO PARTICIPATE?
There is no cost to you for taking part in this study. The newer kind of electrodes with 32 channels on a big film will be provided free of cost by the manufacturer as part of the study.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?
In the event of physical injury resulting from your participation in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. There is no program in place for other monetary compensation for such injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?

For questions about the study, contact the researcher, Dr. Thomas Nowak, at 317-948-9227. After business hours, please call 317-944-5000 and ask for the GI fellow on call.

In the event of an emergency, you may contact Dr. Nowak at 317-944-5000.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Subjects Office at 800-696-2949 or at irb@iu.edu.

CAN I WITHDRAW FROM THE STUDY?

If you decide to participate in this study, you can change your mind and decide to leave the study at any time. The study team will help you withdraw from the study safely.

Your participation may be terminated by the investigator without regard to your consent if he feels that continuation in the study may affect your health or personal welfare.

PARTICIPANT'S CONSENT: Phase 1
In consideration of all of the above, I give my consent to participate in the phase 1 part of this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____**Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____**Date**:_____

PARTICIPANT'S CONSENT: Phase 2
In consideration of all of the above, I give my consent to participate in the phase 2 part of this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____**Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____**Date**:_____

PARTICIPANT'S CONSENT: Phase 3 (taking images and video of the surgical procedure of placing the stimulator)
In consideration of all of the above, I give my consent to participate in the phase 3 part of this research study. I will be given a copy of this informed consent document to keep for my records. I agree to take part in this study.

Participant's Printed Name:_____

Participant's Signature:_____**Date**:_____

Printed Name of Person Obtaining Consent:_____

Signature of Person Obtaining Consent:_____**Date**:_____