University of Pittsburgh

Department of Anesthesiology

TITLE: A Pilot Study Assessing the Feasibility of Implementing TMC-CP01 treatment based on the VANISH (Virtual Autonomic Neuromodulation Induced Systemic Healing) system in reducing pain and opioid requirement in subjects suffering from Chronic Low Back Pain (CLBP) (VANISH Study)

KEY INFORMATION

You are being asked to take part in a research study. Research studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision.

- The purpose of this research is to evaluate whether a wearable Virtual Reality (VR) device helps to reduce the need for opioid pain medication in patients suffering from chronic low back pain (CLBP).
- The duration of this study is 8 weeks.

Once you are enrolled into the study, you will be randomly (like a flip of a coin) assigned to either the intervention group or control group. We cannot predict or influence the group in which you will be randomized.

Intervention group
Half of the subjects (10 subjects) will receive the virtual reality (VR) intervention every day for 8 weeks in addition to their current opioid prescription and weaning guidelines. This VR intervention will communicate with an app on your smartphone and data from this app will be transferred and stored in Amazon Web Services. This group will also be asked to participate in an online focus group discussion after all intervention participants have completed the study. The online focus group allows subjects to discuss their experiences with the VR system.

Control Group
The other half of subjects (10 subjects) will receive only their current opioid prescription and the same weaning guidelines and are considered to be in the "control group". You will input your daily pain and medication requirement into an app uploaded to your smartphone. The data from this app will be transferred and store at Amazon Web Services. Those in the control group will be given the opportunity to try the VR system at the end of the study.
The risks and benefits of the study are:

- *Study device:* Bumping into objects, furniture, or other physical barriers.
- *Opioid-Weaning:* You may report increased psychological withdrawal, such as craving, or more pain.
- *Collection and storage of private health information:* There is a risk of breach of confidentiality of your private health information obtained from your medical record.

The possible benefit is that you may find that the VANISH system may help you wean from opioid more effectively then by standard of care measures alone.

You may choose not to participate and continue to have your pain and medications managed by your health care team.

CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

TITLE: A Pilot Study Assessing the Feasibility of Implementing TMC-CP01 treatment based on the VANISH (Virtual Autonomic Neuromodulation Induced Systemic Healing) system in reducing pain and opioid requirement in subjects suffering from Chronic Low Back Pain (CLBP) (VANISH Study)

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About this consent form
Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form. If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Why is this research study being done?
Chronic pain affects an estimated 100 million Americans, around one-third of the U.S. population. One of the most common chronic pain conditions is Chronic Low Back Pain (CLBP), which is the leading cause of disability in the world. Opioid pain medications such as oxycodone and codeine are the most common treatments for CLBP. However, patients taking opioids can become dependent on them and require higher doses to achieve pain relief. Given these risks, there is a clear need to develop effective ways to treat chronic pain without using opioids.

This research study will compare two treatments for patients with chronic low back pain who are currently taking opioid medication:

1. **VR Treatment**: Daily sessions of Virtual Reality with biofeedback
2. **Control**: Usual care with a pain medicine physician

Who is being asked to take part in this research study?
You are being invited to participate in this research study because you are 18 years of age or older and have been diagnosed with CLBP and are planning to reduce your opioid medication use.

How long will I take part in this research study?
Both the VR Treatment and Control group will take part in the study for 8 weeks. Everyone who participates in this study will attend a total of three study visits. Study Visit 1 will take place at the UPMC Pain Medicine Clinic at Centre Commons, while Study Visit 2-3 can be done in-person or through phone. These visits will be approximately 1-2 hours long.

In the rare case that you experience technical difficulties using the equipment or virtual reality app, the study team may decide to extend your participation, in which you may choose whether or not to do so. The extension may range from a few days to several weeks.

What will happen in this research study?
Half of the subjects who are enrolled will be randomly assigned to the VR Treatment group, and the other half will be assigned to the Control group. The subjects assigned to the VR Treatment will receive the VANISH virtual reality intervention every day for 8 weeks in addition to their current opioid prescription and opioid weaning guidelines. The Control group subjects will receive only their current opioid prescription and the same weaning guidelines. Both groups will use the Flowly smartphone app to collect pain information.

Study Visit 1 (Week 0)
The Screening Visit will take about 2 hours at the UPMC Pain Medicine Clinic at Centre Commons. At this visit, you will:

- Meet with study doctor to collect demographic information, medical history and current medications.
- Sign a standard Opioid Use Agreement if you agree to do opioid weaning.
- Give you a urine test to assess the type and volume of opioids you are using now (optional).
- Give you a salivary cortisol test by placing an absorbent swab in your mouth (optional).
    - Cortisol is a hormone our bodies make in response to stress and can be measured in saliva. (Please see the pictures below)
- Give you 9 online questionnaires to fill out regarding your feelings about treatment and the future, opioid cravings, recent behaviors, opioid withdrawal symptoms, attitudes, opinions, pain history and levels, stress levels, and anxiety levels.
- If you have an iPhone version 6s/6s+ or newer, we will help you download the Flowly app to your smartphone. If you do not have an iPhone 6s/6s+ or newer, we will provide you with an iPhone to use for the duration of the study.
- Teach you how to use the Flowly app and **(VR Treatment only)** virtual reality VANISH system on your phone

Figure 1. Saliva cortisol sample.

Salivary Cortisol

To prepare for the collection of your saliva:

- **24 hours before collection** – do not use any lotions that contain steroids such as hydrocortisone. Steroid inhalers should not be used prior to collection as well.
- **30 minutes before collection** – do not eat or drink anything 30 minutes before collecting saliva.
- Consult with study physician if your gums or inside of your mouth are bleeding prior to collecting the sample. This may contaminate the sample and interfere with results.

Opioid Weaning

The study doctor will work with you to help you voluntarily reduce your daily short- and long-acting opioid dose(s) by approximately 15% over a 4-week period. Your opioid prescription(s) will also reflect these changes. This slow and shared decision-making process will be repeated at study Visit 1 and 2, as tolerated. You can wean faster and come off opioids altogether if you like. You will receive weekly text messages to complete online surveys about your opioid use, cravings, pain, anxiety, and stress levels. Research staff will be available via phone and text messages to provide technical support. You may contact research staff for support at any time.

VR Sessions

Subjects in the **VR Treatment** group will use a device called a VR Shinecon, which is a virtual reality-enabled pain management system based on the VANISH (Virtual Autonomic Neuromodulation Induced Systemic Healing) system and method. VANISH is designed specifically for pain management and is tailored for low back pain. The VANISH system is designed as a game in which your body is the controller. By using heart rate and respiration signals to control characters and objects in real time in VR, you gain greater awareness and control over your physiology. The games are designed to guide your body to a better state for pain reduction. This can happen by increasing or decreasing your heart rate and breathing slowly and deeply. The goal of VANISH is to train you to automatically adjust the way your body feels in order to improve your pain. By providing an accessible and effective pain management tool, it is possible you can reduce or avoid opioid use, dependency, and resulting complications due to using opioids. The VR delivery of the VANISH system is not approved by the Food and Drug Administration (FDA).

The **VR Shinecon device** is shown in the picture at right and is similar to wearing a mask over the eyes and part of the nose. You will also wear **headphones** and a **heart and respiratory rate sensor** on your ears. This study also requires an iPhone 6s/6s+ smartphone to operate the VR system, which fits inside the headset. When a VR session is activated:

- The Flowly app will prompt you to answer the pre-session questions, which include pain, stress, and anxiety levels.

- The app will prompt you to connect the sensors and will wait until there is a successful connection. Once the sensors are paired via Bluetooth, the VANISH system will capture your respiration and heart rate.
- You will then be prompted to start the session. Brief audio instructions will be worked into each VR session to explain the exercises and educate you on how they help with pain management.
- After the treatment is finished, the app will prompt you to answer the follow up questions.
- Once the session is finished, the app will upload your answers and session information to a database. Pre- and post- session questions will allow you to keep track of your own recovery and allow our research team to log your data for later analysis.

Figure 2. User with VANISH system.

Study Visit 2 (Week 4)
Visit 2 will take about 1.5 hours. This visit can be done in-person at the UPMC Pain Medicine Clinic or via phone. At this visit, we will:

- Meet with study doctor to follow-up about opioid weaning, your progress using virtual reality, and to answer any questions you have.
- Give you 9 online REDCap questionnaires to fill out.
- Collect a urine drug screen test and a salivary cortisol test (optional).
    - Urine drug screen test and salivary cortisol collection are optional. Those who do this visit via phone call will not need to do the urine drug screen tests or salivary cortisol collection.

Visit 3 (Week 8)
Visit 3 will take about 1 hour at the UPMC Pain Medicine Clinic at Centre Commons. At this visit we will:

- Meet with the study doctor to talk about your progress and to answer any questions you have.
- Give you 9 online REDCap questionnaires to fill out.
- Collect a urine drug screen test and a salivary cortisol test (optional).
    - Urine drug screen test and salivary cortisol collection are optional. Those who do this visit via phone call will not need to do the urine drug screen tests or salivary cortisol collection.
- Ask you to return all VR equipment and/or smartphones from the study.
    - Those who are attending this visit in-person is advised to return all VR equipment during this visit. Subjects who complete this visit via phone will be given up to 3 weeks from their last study visit to return all VR equipment at the UPMC Pain Medicine Clinic. Subjects that are unable to return all VR equipment and/or smartphones will be billed an invoice to their home address.

During this final visit, subjects from the Control group will also be given the option of trying the VR Treatment and will be trained to use the VANISH system for a full 8-week intervention. If you decide to try the VANISH system, you can continue your opioid-weaning plan with the study doctor for this additional 8-week period.

Completion of Study Tasks at Home

Control Group:

- EVERY DAY: Complete one survey in the Flowly App to track of pain, anxiety, and stress levels for 8 weeks.
- Continue opioid weaning plan as discussed with the study doctor.
- ONCE A WEEK: Complete weekly online questionnaires. A link to these questionnaires will be texted to you.

Intervention Group:

- EVERY DAY: Use the VR and biofeedback devices and complete 20-minute sessions for 8 weeks.
    - The VR exercises focus on breathing. You will see objects in a 3D virtual world which will change movements with your breathing. You will be guided to use the exercises in ways that manage your body responses.
    - You will complete all sessions for the remainder of the 2-month trial at your own home. While you will do these sessions yourself, the research team will check that you are using the system by observing the biofeedback readings and device use via electronic data transfer.
    - Tech support will be available 24/7 for VR system users via **email: contact@flowly.world** or **phone number, 917-544-2934.** In certain cases, Tamade may also contact subjects directly if they find issues in data such as physiological measures.
- EVERY DAY: Complete two surveys in the Flowly app, one at the beginning and one at the end of each VR session to keep track of pain, anxiety, and stress levels for 8 weeks.
    - If you use the VANISH system for less than 3 times a week, you will be withdrawn from the study and must return all VR equipment and/or smartphones to the UPMC Pain Medicine Clinic.
- ONCE A WEEK: Complete weekly online questionnaires in REDCap. A link to these questionnaires will be texted to you.

What are the possible risks, side effects, and discomforts of this research study?

(1) VR Headsets Can Lead to Loss of Spatial Awareness
Because the VR device is worn as a headset, it will obstruct your vision. Therefore, you should use the VANISH system only when you are comfortably seated where there is no risk of bumping into objects, furniture, or other physical barriers.

(2) Opioid Weaning May Lead to Increased Physical and Psychological Withdrawal
The study physicians taking over your opioid prescribing will advise you about managing common side effects of opioid use, such as constipation and sedation. Your opioid medication will be reduced (weaned) slowly according to a shared decision between you and the study physician; thus the following withdrawal symptoms will be minimal and occur infrequently. You may report increased *physiological* and *psychological* withdrawal, which will generally be craving, increased pain, tiredness, or headache. While these symptoms are uncomfortable, they

are not dangerous, and you may choose to stop the weaning at any time and still remain in the study.

Some of the symptoms of physical and psychological withdrawal are:

- Restlessness
- Lacrimation (watery eyes)
- Rhinorrhea (runny nose)
- Yawning
- Perspiration (sweating)
- Chills
- Myalgia (muscle pain)
- Mydriasis (dilated pupils)
- Irritability
- Anxiety (nervousness)
- Backache
- Joint pain
- Weakness
- Abdominal cramps
- Insomnia (trouble sleeping)
- Nausea (upset stomach)
- Anorexia (decreased appetite)
- Vomiting
- Diarrhea
- Increased blood pressure
- Increased heart beat
- Faster breathing

(3) Salivary Cortisol Testing May Lead to Discomfort
There is a risk of minor discomfort during the saliva collection.

(4) Before Collecting Saliva, Subjects Must Hold Off on the Use of Steroid Inhalers for 24 Hours

Some of the potential symptoms for withholding steroid inhalers:

- Tiredness
- Joint Pain
- Stomach pain
- Body ache
- Lightheadedness

Since the subjects are withholding steroid inhalers for a short amount of time, the listed symptoms are expected to occur infrequently, and pose minimal risk of harm.

(5) Risks of Questionnaires
There is a risk of personal discomfort while answering questions about opioid use, stress, anxiety, and other sensitive topics. You do not need to answer any question that you do not wish to. You may take breaks or stop at any time.

(6) Risks of Breach of Confidentiality
You will use the Flowly app **daily for 8 weeks**. The app will measure your daily opioid use and pain level. If you are assigned to the VR Treatment group, the VANISH system will also measure your body temperature, heart rate and other related physiological measures. The physiological data will be stored in a database hosted by Amazon Web Services.

There is also risk of breach of confidentiality of your private health information obtained from your medical record. That is, in very rare cases, people not associated with this research study may inadvertently see your identifiable research results. All of your medical record and study-

related information will be considered protected health information and will be kept confidential per the HIPAA privacy act. We will do everything in our power to prevent this from happening by keeping all paper research records in locked files and identifying all specimens and medical information by a subject ID number, rather than by your name. The codebook containing your name and subject ID number will be kept secure by the Study Team.

(7) Unknown Risks
As with any experimental procedure, there may be adverse events or side effects that are currently unknown, and certain of these unknown risks could be permanent, severe or life-threatening.

What are the possible benefits from being in this research study?
You may find that the VANISH system may help you wean from opioid more effectively than by standard of care measures alone.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
You will be promptly notified if any new information is discovered that suggests you were put at any increased risk as a result of your participation in this research study.

What if I want to stop taking part in the study?
You may withdraw, at any time, your consent for participation in this research study. Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

- To formally withdraw your consent for participation in this research study, you should notify your decision to the principal investigator of this research study at the address listed on the first page of this form.
- Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship(s) or medical care at the University of Pittsburgh, UPMC hospitals or affiliated health care providers, or with any health insurance providers.
- If you decide to withdraw from the research study after you have started weaning your opioid medication, no study assessments will be done after you leave the study.

If I agree to take part in this research study, can I be removed from the study without my consent?
It is possible that you may be removed from the research study by the researchers if you are unable to follow the daily tasks required by the study, if any safety concerns arise, or if information is obtained that indicates you do not meet eligibility requirements for inclusion in the study.

Will I be paid to take part in this research study?
Control group will receive up to $150 for completing the study, detailed as follows:
Week 0 (First Visit): $25
Week 4 (Second Visit): $25
Week 8 (Last Visit): $40

VR group will receive up to $200 for completing the study, detailed as follows:

Week 0 (First Visit): $35
Week 4 (Second Visit): $35
Week 8 (Last Visit): $50
Focus group (optional): $20

An extra $30 will be paid for the completion of at least 90% of the daily VR sessions or surveys via Flowly each month, totaling to another $60 in compensation. Those randomized to the VR Treatment group who attend the online focus group will also receive an additional $20.

You will be paid on a reloadable debit card. All study compensation is taxable income regardless of the amount. If you receive $600 or more in a calendar year from one organization, that organization is required by law to file a Form 1099 – Miscellaneous with the IRS and provide a copy to the taxpayer. Individuals who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for 'backup withholding, thus you would only receive 76% of the expected payment.

Your data from this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights, nor will you share in any money that the investigators, the University of Pittsburgh, or outside agencies may receive.

How much will I have to pay to take part in this research study?
The study is provided at no cost to you during the 8-week study. If you did not receive the VR intervention during the study, you have the option of trying the VR system at zero cost. We also will reimburse you for your parking in the clinic parking lot during study visits or bus fare to and from the study site up to a maximum of $35 during the 8-week study.

Neither you nor your insurance provider will be charged for the costs of any of the procedures performed for the purpose of this research study (such as urine testing or salivary cortisol tests). You will be charged in the usual manner for any procedures performed as part of your standard medical care (care you would receive even if you were not participating in this research study). However, if you do not return the VR Shinecon headset device and/or loaned smartphone by the end of the study, you will be billed for the cost of the equipment.

If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff.

What happens if I am injured as a result of taking part in this research study?
University of Pittsburgh researchers and their associates who provide services at UPMC recognize the importance of your voluntary participation in their research studies. These individuals and their staff will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research. If you believe that you are injured as a result of the research procedures being performed, please immediately contact the Principal Investigator listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. It is possible that UPMC may bill your insurance provider for the costs of this

emergency treatment, but none of these costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care unless otherwise specifically stated below. There is no plan for monetary compensation. You do not, however, waive any legal rights by signing this form.

Who will know about my participation in this research study?
Any information about you obtained from this research will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in a locked file cabinet. Your identity on these records will be indicated by a case number rather than by your name, and the information linking these case numbers with your identity will be kept separate from the research records. You will not be identified by name in any publication of the research results. We will attempt to preserve your medical record and participation in this study as confidentially as possible, but breach of confidentiality is a risk of participation.

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; 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.

In the future, the investigators may decide to share data with other investigators both within and outside of this institution. If that were to occur, we would de-identify all of the information prior to sharing any data.

How will my information be transmitted, stored, and used in this research study?

(1) Flowly App Survey Data Will Be Managed Only by Tamade, LLC
You will be asked to download a smartphone app called "Flowly" to answer questions about your personal feelings about treatment. The app will also ask you questions about the future, opioid cravings, recent behaviors, opioid withdrawal symptoms, attitudes, opinions, pain history and levels, stress levels, and anxiety levels. You will download the Flowly app from with the assistance of research staff. Once downloaded, research staff will unlock the app. Then you will register your account using a username, password, and 4-digit pin. Your username can be anything. A unique identifier will be attached to your data instead of your name. Your data will be sent through the internet to a storage database hosted by Amazon Web Services. This data will be accessed only by software developers at Tamade, LLC and University of Pittsburgh research staff. All usage and transference of data will be HIPAA compliant, which means that anything that could identify you will be removed.

(2) VR Device Data Will Be Stored in Amazon Web Services Managed by Tamade, LLC
Your reports of opioid use, pain level, and biofeedback measures will be taken from the VR Shinecon headset device, sent through the internet, and stored in a database hosted by Amazon

Web Services. This data will be accessed by the software developers at Tamade, LLC and University of Pittsburgh research staff. A unique identifier will be attached to your data instead of your name.

(3) RedCap Surveys Will Use a Unique ID to Your Data Instead of Your Name
You will receive weekly questionnaires about opioid cravings and pain, anxiety, and stress levels via email from Redcap. This data will be accessible by University of Pittsburgh research staff and by REDCap software developers. All usage and transference of data will be HIPAA compliant. A unique identifier will be attached to your data instead of your name.

(4) Text Messages Received in this Study Will be Sent and Stored in a Secure System
The text messages you will receive as part of this study are sent from a secure, encrypted system, and all of your responses are stored in the Mosio system. However, the text messages you send are not encrypted or secure during transmission and could be intercepted. Therefore, it is important to understand that your text message response is not protected, and it is possible that it may be viewed by others. It is important to note that depending on your cell phone carrier, even if you delete the text message from your phone, your cell phone carrier will retain those messages for an extended period of time. You are responsible for the security of any information that is stored on your cell phone or mobile device. We suggest you periodically check for and delete any sensitive information that may be contained in these text messages.

(5) Urine Drug Testing Results Will be Processed and Stored Safely by Quest Diagnostics
When you take a urine drug test during your clinic visits, your sample will be processed by Quest Diagnostics. This company requires the following identifiable information in order to process the sample:

- Your printed name and signature on the specimen collection form
- Your study ID number on the sample cup and specimen collection form
- Your date of birth on the sample cup

Quest Diagnostics will receive all the information listed above. Test results will only be accessible by the study doctor or University of Pittsburgh research staff in determining your eligibility for the study.

There are security measures in place to protect your data at all of the organizations listed above. Although we will do everything in our power to protect your data, absolute confidentiality cannot be guaranteed.

Will this research study involve the use or disclosure of my identifiable medical information?
This research study will involve the recording of past, current and/or future identifiable (pertaining to only you) medical information from your hospital and/or other health care provider (e.g. physician office). The information that will be recorded will be limited to diagnostic information, lab results, medications, demographics, and medical history. The information will be used to determine your eligibility for this study and to follow your care once you are enrolled in the study.

We will place your consent form for this study and your tapered opioid prescription into your medical record, but no other data from the study will be placed into your UPMC medical records.

Who else will have access to identifiable information related to my participation in this

research study?
In addition to the investigators listed on the first page of this consent form, the research staff, and the organizations listed in the previous section, the following individuals will or may have access to identifiable information related to your participation in this research study:

- Authorized representatives of the University of Pittsburgh Office of Research Protections may review your identifiable research information (which may include your identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study.
- If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.
- Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).
- Individuals from the National Institutes of Health and the Food and Drug Administration will be able to access research data, including your private health information for purposes of monitoring the research. Although these organizations have safeguards to protect your privacy, we cannot guarantee the confidentiality of your health information after it has been obtained by those organizations.

We will protect your privacy and the confidentiality of your research records, as described in this document, but cannot guarantee the confidentiality of your research records, including information obtained from your medical records, once your personal information is disclosed to others outside UPMC or the University.

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?
The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for an indefinite period of time. Your authorization will last indefinitely as well. Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following final reporting or publication of a project.

May I have access to my medical information that results from my participation in this research study?
In accordance with the UPMC Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your participation in this research study) contained within your medical records filed with your health care provider.

A description of this clinical trial will be available on https://www.clinicaltrials.gov/, as required by US 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.

Your rights as a research subject
Your participation in this research study is completely voluntary. Whether or not you provide your consent for participation in this research study will have no effects on your current or future relationship with the University of Pittsburgh, your current or future medical care at a UPMC hospital or affiliated health care provider, or your current or future relationship with a health care insurance provider.

To formally withdraw your consent for participation in this research study, you should provide a written and dated notice of this decision to the principal investigator at the address listed on the first page of this form.

If you have any questions about your rights as a research subject or wish to talk to someone other than the research team, please call the **University of Pittsburgh Human Subjects Protection Advocate toll-free at 866-212-2668**.

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VOLUNTARY CONSENT
The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by a qualified individual or by the principal investigator listed on the first page of this consent document at the telephone number given. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.

I understand that I may contact the **Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668)** to discuss problems, concerns, and questions; obtain information; offer input; or discuss situations in the event that the research team is unavailable.

By signing this form, I agree to participate in this research study and to authorize Dr. Mahajan and the members of his research team to use my medical record as described in this document. A copy of this consent form will be given to me. Also, I further certify that no research component of this protocol was begun until after the consent form was signed.

_____	_____	_____
Participant's Signature	Printed Name of Participant	Date/Time

CERTIFICATION of INFORMED CONSENT
I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____

Printed Name of Person Obtaining Consent   Role in Research Study

____________________________________   _____________

Signature of Person Obtaining Consent   Date/Time