Thalamic Deep Brain Stimulation for the Treatment of Refractory Tourette Syndrome

NCT01817517

2/25/2021

If appropriate for this study, a scanned copy of the signed consent form should be uploaded to the participant's Epic/EMR record.

Patient I.D. Plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: Thalamic Deep Brain Stimulation for the Treatment of Refractory Tourette Syndrome

Application No.: NA_00073086

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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

- 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.
- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.
- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.
- If children and adults can join this study, the word "you" in this consent form will refer to both you and your child.
- The person being asked to be in this research study may not be able to give consent to be in this study. You are therefore being asked to give permission for this person to be in the study as his/her decision maker.
- A statement will be added to your medical record that you are in this research study. Results from any clinical tests you have will be included in your medical record. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.

2. Why is this research being done?

This research is being done to try to understand if the use of deep brain stimulation or DBS can treat the symptoms of Tourette syndrome that do not respond well to current medications. In order to do this we will need to place a very small needle called electrode in a specific part of the brain that we think may alter the abnormal activity in the brain responsible for your symptoms.

The Food and Drug Administration (FDA) has approved DBS for treatment of Parkinson's disease and obsessive-compulsive disorder although for this last disorder efficacy has not been proven yet. The FDA has not approved DBS for use in people with Tourette syndrome, and Medtronic (the manufacturer of the device) has not conducted testing for the system in Tourette syndrome. Therefore its use in this study is investigational and we do not know if you will benefit.

The primary implantable pulse generators used in this study are derived from the Medtronic Activa deep brain stimulation system, including the PC and RC 2-channel pulse generator models. As of April 1st, 2021, Medtronic will no longer provide the Activa PC for new or replacement implantations, but will support the Percept model implantable pulse generator. New implantations for this protocol in Tourette Syndrome will also only utilize the Percept model pulse generator.

People with severe Tourette syndrome may join.

How many people will be in this study?

A total of 10 people will participate.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things:

- Before you sign this consent form, you will go through an interview with a psychiatrist or a neurologist who will assess your capacity to give consent to this study. After your capacity to give consent has been established you will have to come in for 3 consecutive visits one week apart.

In order for you to have the capacity to give consent, you must have an adequate ability to reason, and understand the information contained in this consent form. If at any time, you are confused about statements in this form, please ask for more information or clarification. Other impairments of reasoning may exclude you from the capacity to give consent including intellectual or emotional immaturity, severe mental retardation, severe mental illness, sleep deprivation, medication side effects, or intoxication.

Some of the testing described below will be videotaped. The videotaped tests will include your face and your body. It is necessary to videotape your body and face because the motions and expressions of the body and the face are crucial to understand the motions and emotions associated with TS and OCD. The videotapes may be looked at by other researchers or clinicians who are unfamiliar with you. The videotapes will also be used for clinical, research, and teaching purposes. Your name will be deleted from videotapes before the videotapes are presented at meetings or published in journals.

If you are between the ages of 15-20, a caregiver or family member must accompany you to all of the study visits described below.

If you are less than the age of 25, an additional Ethics Committee Consultation will be obtained from the hospital to seek permission for continuing with the study in your particular case.

If you are between the ages of 15-18, your parent or guardian will be required to sign consent for you to participate in the study.

If you are under the age of 18, your parent or guardian will be informed if we believe any of our findings indicate that you may cause harm or injury to yourself or others. However, parents/guardians will not be told about other behaviors we may find out about, including alcohol consumption or your sexual activity unless it may represent a danger to you or others.

Visit #1

- A psychiatrist or neurologist will confirm through an interview with you and a review of your records that you have Tourette syndrome.
- You will be asked questions regarding your medical history including review of medical records, current medications and duration of prior medication trials.
- You will go through a complete physical examination including height, weight and vital signs.
- EKG, blood samples for clinical laboratory tests (a total of about 3 ½ teaspoons of blood will be collected) and urine sample for urine toxicology screen and urine pregnancy test (for females capable of having children) will be obtained. You cannot take part in this study if you are pregnant or if your urine tests positive for illicit substances.
- Tourette syndrome symptom scales will be filled out, and you will undergo a neuropsychological evaluation.
- You will be referred to your medical physician for a pre-operative evaluation to determine if you are safe to undergo surgery and anesthesia

The visit may last up to 2 hours.

Visit #2

At this visit, the following assessments will be performed:

- We will fill out again Tourette syndrome symptom scales and you must continue to meet score requirements, which means that your symptoms must be severe in order to remain in the study.
- A urine sample for urine toxicology screen and urine pregnancy test will be collected.
- You will be asked several questions concerning your mood and emotional well-being.

The visit may last up to 3 hours.

Visit #3

At this visit, the following assessments will be performed:

- We will repeat Tourette syndrome symptom scales and as the previous week you must continue to meet requirements to remain into the study which means that your symptoms must be severe.
- A urine sample for urine toxicology screen and urine pregnancy test will be collected.
- We will schedule a pre-operative MRI scan. This scan will help us to place the electrodes during surgery.
- You will again be asked several questions concerning your mood and emotional well-being.

As part of your participation in this research study, you will have an MRI exam. The MRI exam will take approximately 30 minutes. Prior to your exam, you will be asked to complete a standard questionnaire. The purpose of this questionnaire is to ensure that you are able to safely enter the MRI area. If you have a history of metal in your head or eyes, you cannot take part in this study.

To start your MRI test, you will lie on a padded table. The table on which you are lying will be moved to the center of an MRI magnet, which looks like a long narrow tube. Even though the tube is open, some people feel confined in small places. If this bothers you, please notify the MRI staff. You may end your participation in this study at any time by telling the MRI staff. When MRI pictures are taken, radio-signals and magnetic fields are used. When this happens, it is normal for the MRI machine to make loud, banging, and clicking noises. You will be asked to wear earplugs or headphones for your comfort during the exam.

During the exam, the MRI staff is able to see and hear you. You will be able to hear the MRI staff. The MRI staff will be talking to you throughout your MRI exam and may issue simple instructions regarding holding your breath, maintaining position, etc. You will generally be requested to lie perfectly still throughout the exam.

Incidental Findings:

The MRI you are having as part of this research study will be reviewed by a qualified person just as it would be if you were having the MRI as part of your routine medical care.

There is a possibility that while reviewing your MRI we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by mail or by phone. In the case of a potential serious emergency, someone may go to your home.

A qualified person (usually a member of the research team) will talk to you if there is an incidental finding. You do not have an option to decline information about an incidental finding.

If you want, we will give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

- An incidental finding may cause you to feel anxious.
- Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance.
- The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

The visit will last less than 1 hour.

At the conclusion of this visit, if you continue to meet all study inclusion criteria you will be given an appointment card for the next study visit. **The next study visit is the neurosurgical procedure for implantation of the DBS device.** The neurosurgical procedure will be planned within 1-2 weeks after Visit #3.]

It is our intention that this device is left in you, unless removal is clinically indicated.

Visit #4 – Neurosurgical Procedure for Implantation of DBS System

At this visit, the device will be implanted by the neurosurgical study team according to standard operating procedure utilized for implantation of DBS for patients with Parkinson's.

You will need to be admitted to the neurosurgery floor of the Johns Hopkins Hospital for 3 days. You will be asked to sign a separate hospital/surgical consent form. You will have surgery to place electrodes (plastic and metal tubes of diameter 1/16-1/32 inch) in the brain. The surgery itself will be performed with intravenous sedation only. An anesthesiologist will always be present in the operating room in the event of an emergency.

An additional MRI will be obtained the morning of the surgery. This scan will be performed while you are wearing a stereotactic frame applied by the neurosurgeon just prior to the exam. The frame will remain in place during the entire implantation procedure.

A recording device will be used along with the MRI scan results obtained from the morning of surgery in order to place the electrode.

Fluoroscopy (an imaging procedure involving radiation that can see movement) will be used to verify the final position of the electrode.

A head CT examination will be obtained at the end of the placement procedure, again to assess the placement accuracy and safety.

Visit # 5 – Implantation of the Pulse Generator

About one week after the neurosurgical procedure, you will return for implantation of the pulse generator (the "battery") under the chest wall. The intracranial electrode will be connected to the pulse generator which supplies power to the electrode. The DBS lead cables are tunneled behind the ears and connected to the lead extension cables. The lead extension cables are tunneled under the skin to the collarbone pocket housing the pulse generator. The pulse generator itself is attached to the underlying tissue that covers the muscle (pectoralis fascia) with stitches to avoid it flipping in the pocket.

The study neurologist (with experience in programming DBS devices who has extensive experience working with patients with movement disorders undergoing DBS) in conjunction with the study psychiatrist will set the initial stimulation parameters. The neurologist in conjunction with the psychiatrist will use Tourette syndrome symptom scales, acute changes in your symptoms and/or appearance of adverse events thought likely to be related to DBS to optimize programming at all subsequent follow-up visits.

Up to 4 weeks will lap between visit 5 and 6 in order for us to assess if any change in your clinical condition is due to the surgical procedure by itself.

You will also be provided with a patient controller device that will allow you to turn the device on or off at home if needed.

Deep brain stimulation pulse generators typically have a battery lifetime of between 3-5 years, this may become shorter for your case if the current required to control your symptoms is relatively high. Exchanging the pulse generator for a new one requires a brief operative procedure, typically performed with local anesthesia and sedation.

A follow-up MRI will be ordered at this time. This scan will take place before Visit #6 (the first programming visit) to more accurately assess the lead placement before the programming session.

Visits #6 – 9 – Follow-up/Optimization of Programming

You will come in for a follow-up visit every week after implantation of the pulse generator for 4 consecutive weeks. At each visit the study neurologist in conjunction with the psychiatrist will use Tourette syndrome symptom scales, acute changes in symptoms and/or appearance of adverse events likely to be related to DBS to optimize programming at all subsequent follow-up visits. You will also answer questions about mood and emotional health, and at several visits undergo further neuropsychiatric testing.

Visits #10 – 12: Follow-Up Visits

The purpose of the follow-up visits is to monitor for symptom changes, report any complications and to optimize programming if necessary.

You will come in monthly after implantation of the pulse generator. The neurologist in conjunction with the psychiatrist will use Tourette syndrome symptom scales, acute changes in your symptoms and/or appearance of adverse events likely to be related to DBS to optimize programming. At 3 and 6 months after the implantation of the pulse generator we will test again your attention, memory and learning capability to assess any improvement or worsening in relation to DBS. You will also answer questions about mood and emotional health, and at several visits undergo further neuropsychiatric testing.

Reprogramming of the device will be implemented as needed on the basis of the development of adverse events (i.e. infections) or your clinical condition at the time of the visit (worsening of your symptoms, lack of tolerability for the device).

A urine toxicology screen will be done to monitor if any changes in symptoms may be due to use of illicit drugs.

Last Visit – Study Completion

The purpose of this last visit is to monitor for symptom changes, report any complications and to optimize programming if necessary.

The study neurologist in conjunction with the psychiatrist will use Tourette syndrome symptom scales, acute changes in obsessive compulsive disorder (OCD) symptoms, acute changes in attention deficit hyperactivity disorder (ADHD) symptoms and/or appearance of adverse events deemed likely to be related to DBS to optimize programming at all subsequent follow-up visits. A final test of your attention, memory and learning capability will be done. A urine toxicology screen will be also done to monitor if any changes in symptoms may be due to illicit drug use. You will also answer questions about mood and emotional health, and undergo further neuropsychiatric testing at this final visit.

At the end of this visit, you will be discharged from the study and will continue standard clinical care for patients who undergo DBS procedures. We will continue to collect any adverse event related to the study even after you are formally discharged from it one year after the implant. You will continue to meet with the psychiatrist and neurologist who will closely coordinate care. You will be coming to the psychiatrist or neurologist office on a monthly basis or as needed.

Future necessary procedures after the conclusion of the study may include:
1) turning off of the device,
2) complete removal or explant of the device,
3) replacement of the device and
4) reprogramming of the device.

These measures will be implemented as needed on the basis of the development of adverse events (i.e. infections) or your clinical condition at the time of the visit (worsening of your symptoms, lack of tolerability for the device).

If you wish the device to be removed at any time, the study doctor will arrange for this to take place.

Long-Term Follow-Up Visits

The purpose of the long-term follow-up visits is to monitor for additional symptom changes you may experience or to assess any problems you may be having with the implanted device after the formal study visits have concluded. These visits will also be used to optimize programming if necessary over the lifetime of the implanted system. These long-term follow-up visits will occur at 6 month intervals for 2 years after Visit #13, and then annually after that. The visits will occur until you no longer want to participate in the study, or until the device is removed due to a complication or for your wishes, or until the device generator depletes and you no longer wish to have it replaced.

Replacements for neurostimulator (battery portion of the device) will be performed when the battery is depleted as determined during follow-up visits or after changes in symptoms. The first neurostimulator implanted at Visit #5 will be the Activa PC (standard cell). Either the Activa PC (standard cell) or the Activa RC (rechargeable system) will be offered at the times of neurostimulator replacement subsequent to this, depending on your preference and willingness to participate in the recharging process. The RC system will be discussed with you particularly in cases where the lifetime of the prior neurostimulator was less than 2 years.

How long will you be in the study?
You will be in this study for one year after the device has been implanted for the formal study visits, and then semiannually (2 years) and annually for long-term follow-up visits.

4. What are the risks or discomforts of the study?

DBS Implant:
The risks of this study are the same as for brain surgery in general: bleeding, suffering a stroke, paralysis (or lack of movement in the arms and/or legs), death, infection, and risks of anesthesia such as heart attack or allergic reaction.

The risks associated with DBS stimulation itself are failure of therapy, neurologic symptoms including muscle contractions, flashing lights, electric jolting sensations, and altered ability to think or remember. Most of these can be reversed by adjusting the pattern of stimulation.

There is a small but serious risk of intracranial hemorrhage (bleeding in the brain) with implantation of the electrode. The rates of symptomatic and asymptomatic intracranial hemorrhage in DBS are ~ 2% and 1.2%, respectively and infection occurs in ~ 2% of cases. The mortality rate for the procedure is below 1% and is mostly due to intracranial hemorrhage. One large multicenter report of 1,183 patients who received DBS reported a 30-day postoperative mortality rate of 0.4%.

A summary of the Adverse Events related to the therapy, device, or procedure can include: stimulation not effective, cognitive disorders (disorders of thinking or decision making), pain, dyskinesia (abnormal involuntary movements), dystonia (abnormal sustained muscle contractions or postures), speech disorders including dysarthria (difficulty with articulation), infection, paresthesia (uncomfortable tingling sensations), intracranial hemorrhage (bleeding in the brain), electromagnetic interference, cardiovascular events (heart attacks or heart rhythm problems), visual disturbances, sensory disturbances, device migration, paresis/asthenia (weakness/fatigue), abnormal gait, incoordination, headaches, the need for lead repositioning, the need for device removal, hemiplegia (loss of strength on one side), lead fracture or breakage, seizures, respiratory events, and shocking or jolting sensation. The DBS System may be affected by or adversely affect medical equipment such as cardiac pacemakers or therapies, cardioverter/ defibrillators, external defibrillators, ultrasonic equipment, electrocautery, or radiation therapy.

Also, medical equipment used for deep tissue heating (diathermy) for muscle relaxation or other medical therapies should not be used. Methods used to produce deep tissue heating include shortwave diathermy, microwave diathermy and therapeutic ultrasound diathermy. These methods are contraindicated because it is possible the heating energy may be transferred into the deep brain stimulation system components, inducing tissue damage in the brain causing severe injury or death. The deep brain stimulation system itself may also be damaged by the diathermy equipment.

Psychiatric adverse events associated with DBS:
DBS will be discontinued if you experience a worsening of any Tourette syndrome, OCD, or ADHD symptoms without returning to baseline (prior to DBS implantation) within 4 weeks from the worsening of the symptoms.

You will be monitored throughout the study for suicidal thoughts. DBS will be discontinued if you experience depressive symptoms including suicidal thoughts or mania that do not improve with turning off the stimulator.

DBS will be discontinued if you experience depressive symptoms including suicidal ideation or mania that do not improve with turning off the stimulator. DBS will also be discontinued if neurologic symptoms including muscle contractions, flashing lights, electric jolting sensations, increase in involuntary movements do not improve with stimulator setting change and they are severe enough to interfere with your daily functioning. Finally DBS will be discontinued if patients are unable to tolerate the stimulator for any reason not foreseen by the investigators and that clearly interferes with your functioning.

Removal of the implant or explantation may occur in the context of infections involving the pocket under the collar bone housing the implantable pulse generator, or lead cabling over the skull.

Rarely, in the case of infections affecting only the pulse generator it is possible to explant this device along with the extension cabling which terminates at a separate incision behind the ear. In this situation, it is sometimes possible to disconnect the extension cabling from the primary DBS lead cabling at incision. The primary DBS leads are then left in place, and antibiotic therapy is started. However, frequently the infection continues to spread to affect the DBS lead itself, necessitating its removal. The more typical situation involving infections requires the removal of the entire bilateral system, including the components implanted into the brain. Persistent cerebrospinal fluid leakage after this type of surgery, albeit extremely rare, can also lead to an infection requiring explantation. Device removal or component replacement may also be required for lead breakage, disconnection, or poor impedance problems caused by loose connections. Removal of the pulse generator will also occur when the generator has depleted, and a replacement will be placed in the chest pocket under the collar bone and reconnected to the existing implanted cabling.

To minimize risks after the implant subjects will be provided with an ID card that contains information about the system and phone numbers to be reached at any time.

MRI: The effects of magnetic fields in an MRI scanner have been extensively studied, and there are no known significant risks with an MRI exam. You may, however, be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the procedure. You will be asked to wear earplugs or earphones while in the magnet. You may not participate in this study if you have a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices. It is important for you to tell the MRI staff if you have had brain surgery for a cerebral aneurysm or have a metal clip in your brain, or if you have implanted medical or metallic devices, shrapnel, or other metal, such as metal in your eye. If you have a history of metal in your head or eyes, you cannot participate in this study.

MRI with Implant: Although some MRI procedures can be performed safely with an implanted DBS System, MRI use should carefully be weighed. MRI can cause induced voltages in the neurostimulator and/or lead possibly causing uncomfortable jolting, or shocking levels of stimulation. It is contraindicated for patients to be exposed to MRI using a certain radiofrequency coil and head-coil that extends over the chest area. Performing MRI with this equipment can cause tissue lesions from component heating, especially at the lead electrodes, resulting in serious and permanent injury including coma, paralysis or death. To minimize this risk, patient will be issued an ID card specifying risks associated with MRI procedures. The MRI sequences used during the scan before Visit #6 will satisfy the manufacturers safety requirements.

Radiation Exposure: This research study includes exposure to radiation from x-rays or gamma rays. This radiation exposure is for research purposes only and is not part of your medical care. X-rays and gamma rays from natural or medical sources can damage the genetic material (DNA) in your cells. At low doses, the body is usually able to repair the damage.

The radiation exposure that you will get in this research study is 0.3 rem (a rem is a unit of absorbed radiation). This is equal to the 0.3 rem that the average person in the United States gets each year from natural sources like the sun, outer space, air, food and soil. It is less than the 5 rems of radiation that is allowed each year for people who are exposed to radiation in their jobs.

The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other tests outside of this study that are a part of your medical care. If you have questions about the total amount of radiation you will be receiving, you should ask your doctor.

Clinical interview and tests: You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

Blood Draw: Taking blood may cause discomfort, bleeding or bruising where the needle enters the body. In rare cases, it may result in fainting. There is a small risk of infection

Confidentiality
There is the risk that information about you may become known to people outside this study

We may disclose identifiable information about you as described in Section 12 of this form or in other cases. For example, the government including the FDA may see your information if it audits us, and the research team will voluntarily comply with Maryland disclosure laws and will tell the local or state authorities:

- if they suspect abuse or neglect of a child or dependent adult;
- if certain diseases are present; and
- if the team learns that you plan to harm someone. In this case, the team also may warn the person who is at risk.

Additionally, there may be unknown or unforeseen risks associated with participation in the study not listed here.

There may be additional side effects and discomforts that are not yet know.

5. Are there risks related to pregnancy?

This research may hurt an embryo or fetus in ways we do not currently know. You cannot take part in this study if you are pregnant.

6. Are there benefits to being in the study?

There may or may not be a direct benefit to you from being in this study. If you take part in this study, you may help others in the future.

7. What are your options if you do not want to be in the study?

You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected. The alternative to the type of treatment we are proposing is for you to continue with all of your current treatments for TS and the associated co-morbid conditions, including non-pharmacological treatments.

8. Will it cost you anything to be in this study?

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).
- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you be paid if you join this study?

No.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- You fail to follow instructions.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it already has if the information is needed for this study or any follow-up activities.

If you are removed from the study early, your device will be turned off.

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study. If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers.

- You will be asked to give us a list of other health care providers that you use.

14. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people. The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you will not give up any rights you have to seek compensation for injury.

15. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?

Call the principal investigator, Dr. Dean at 443-923-4100. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

c. What should you do if you are injured or ill as a result of being in this study?

If you think you are injured or ill because of this study, call Dr. Dean at 443-923-4100, or Dr. Anderson at 443-287-4561 during regular office hours.

If you have an urgent medical problem related to your taking part in this study, call Dr. Anderson at 781-708-5137 during regular office hours and at 781-708-5137 after hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?

Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

16. Assent Statement

This research study has been explained to my child in my presence in language my child can understand. He/she has been encouraged to ask questions about the study now and at any time in the future.

17. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form; you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time
Signature of Person Obtaining Consent	(Print Name)	Date/Time
Signature of Parent	(Print Name)	Date/Time
Signature of Legally Authorized Representative (LAR) **For CHILD PARTICIPANT**	(Print Name)	Date/Time
Description of LAR's authority under state or applicable local law to act as surrogate health care decision-maker for child research participant (for example, Legal Guardian, court-ordered representative)		Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

Signature of Participant, LAR or Parent/Guardian	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider (Print Name) Date/Time

Signature of Participant (Print Name) Date/Time

Signature of Parent (Print Name) Date/Time

Signature of Legally Authorized Representative (LAR) (Print Name) Date/Time
For CHILD PARTICIPANT

Description of LAR's authority under state or applicable local law to act as surrogate health care decision-maker for child research participant (for example, Legal Guardian, court-ordered representative) Date/Time

Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required) (Print Name) Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR AND A COPY MUST BE GIVEN TO THE PARTICIPANT. IF APPROPRIATE FOR THIS STUDY, A SCANNED COPY OF THE SIGNED CONSENT FORM SHOULD BE UPLOADED TO THE PARTICIPANT'S EPIC/EMR RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).