Informed Consent Form

Project Title: The Human Thalamocortical Network in Tourette Syndrome

ClinicalTrials.Gov NCT:02056873

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UF Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and
AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

Please read this form which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of participant ("Study Subject")

_____

2. What is the title of this research study?

The Human Thalamocortical Network in Tourette Syndrome

3. Who do you call if you have questions about this research study?

Principal Investigator: Michael S. Okun, MD (352) 273-5550

Contact information for emergencies after hours or on weekends or holidays: (352) 265-8408, ask for the neurologist on call and reference this study and principal investigator

4. Who is paying for this research study?

The sponsor of this study is the Center for Movement Disorders and Neurorestoration at University of Florida. Study funding is also being provided by the National Institutes of Health and the National Science Foundation. Medtronic is providing the hardware.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, and how long will you be involved?

The purpose of this study is to learn how deep brain stimulation affects motor and vocal tics associated with severe Tourette Syndrome that is not adequately controlled with medication. The study period is 36 months, or 3 years.

b) What is involved with your participation, and what are the procedures to be followed in the research?

If you participate in this study, you will be screened for surgical candidacy and if eligible, you will undergo implantation of two leads deep into your brain and 2 brain sensors (cortical strips) on the top of your brain. You will be awake during this procedure. You will come back about a month later to have one battery placed in your chest, under general anesthesia, that will control the stimulation produced by these leads. The brain sensors allow the research team to evaluate brain activity that may be related to your tics, and the leads provide stimulation to hopefully reduce frequency and severity of your tics. You will return to our clinic monthly for 3-4 consecutive days at a time for the first 6 months to find your optimal stimulation parameters and for the research team to stream your brain activity captured by the sensors. Ideally, the streamed brain activity will work with stimulation to more efficiently capture your individual tics. After this 6 month period, you will return every 6 months for similar 3-4 day visits to check and reprogram the devices as necessary, until Month 36. The device you receive is rechargeable and is labeled to last 9 years. You will be expected to recharge your device as needed to maintain functionality. The recharging device is called a Recharge Therapy Manager (RTM). You will receive training on how to use this device for recharging your device. You will receive written instructions to take home with you, and you can reach the research team if you encounter any issues.

c) What are the likely risks or discomforts to you?

This study involves 2 surgeries: one awake brain surgery and one outpatient battery placement under general anesthesia. Most likely risks of the first surgery include infection, bleeding in the brain, and discomfort including headache post-surgery. Most likely risks of the second surgery include effects of anesthesia, infection, and soreness post-surgery. Some less likely surgical risks could potentially cause serious injury or death.

Follow up visits may be long and cause fatigue. Some questions asked about your psychiatric history or current experiences may be sensitive and feel uncomfortable.

A complete description of the risks is found in this consent form.

d) What are the likely benefits to you or to others from the research?

You may experience a reduction in severity and/or frequency of your motor and/or vocal tics. Others may benefit from the data provided by your brain sensors, which could illuminate brain networks associated with tics and thereby provide valuable directions for future treatment. Others may also benefit by your results by providing information about the effectiveness of deep brain stimulation for Tourette Syndrome.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

As an alternative to participating in this study, you may opt to continue routine clinical care, including attempts to control tics with medication and/or cognitive behavioral therapy.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study.

Why is this research study being done?

The purpose of this research study is to evaluate the effectiveness and safety of a possible new treatment for Tourette Syndrome (TS). It is a therapy called Deep Brain Stimulation (DBS). The study will also examine the physiology (brain activity) associated with TS and tics and explore the possibility of setting the DBS device to provide responsive brain stimulation (RBS). RBS can be applied when the device can automatically detect a tic by recording an abnormal signal from your brain. The abnormal signal in your brain is detected and the device is set to stimulate to suppress the signal and improve or alleviate your tic(s).

DBS is a surgical procedure that involves putting a wire with tiny stimulating electrodes into each side of your brain. An electrode is a small piece of metal used to take an electric current to or from a power source. These electrodes are connected under the skin to a small electrical unit called a pacemaker (implantable neurostimulator). The pacemaker is similar to a heart pacemaker. In order for your

brain to send messages to your body, it produces a form of electricity. The device sends out electrical impulses that appear to interrupt this flow of electricity. The pacemaker part of the device is located in your chest under the collarbone, in the same place a cardiac pacemaker would be placed. A wire is placed under the skin to connect the pacemaker in the chest to the DBS lead in the brain.

Other surgery options for treating TS involve destroying small parts of the brain within structures called the thalamus or globus pallidus. DBS has the advantage of being adjustable after the procedure is completed. However, like some of the other surgical options, this procedure involves creating holes in the scalp and skull and passing wires to locations deep within the brain.

The use of DBS in the treatment of TS is investigational, which means it has not been approved by the Food and Drug Administration (FDA).

All subjects will receive continuous stimulation through two DBS leads (one on each side of the brain in a structure called the thalamus). During the first 6 months, we will be monitoring information provided by the device. If this information suggests that a physiological signal predictably occurs before your tics and if the FDA approves our proposal, we may change your stimulation from continuous to responsive (RBS). In RBS the device will respond to the signal from the brain and will discharge prior to the tic (responsive stimulation) and therefore the device will not be on all the time.

For this study, we will be using the Medtronic RC+S. It is an implantable, battery powered, computer chip controlled device that can be programmed to deliver stimulation through depth leads (the tiny wires with electrodes) and also through superficial leads; leads we will lay on the top of your brain surface. Providing stimulation to these areas of your brain may relieve symptoms of TS. The pacemaker also records brain electrical activity. Study doctors will use a laptop computer, called the programmer, and a wand to communicate with the pacemaker after it is implanted.

You are being asked to be in this research study because you have a long-standing severe case of TS that has not responded to numerous standard treatments.

Some of the requirements to be in this study are:

a. You must be 21 years of age or older.
b. Your diagnosis of TS must be made by both a neurologist and a psychiatrist and must meet standardized criteria.
c. You must have a minimum score on the Yale Global Tic Severity Scale (YGTSS; 100) Score $\geq$35, and the motor tic subscore $\geq$15.
d. Your symptoms must be causing significant impairment in your functioning, making it impossible or almost impossible to do daily activities, including work or school and interactions with friends and family, causing severe distress and a poor quality of life.
e. Your symptoms have not responded well enough to medications prescribed by a neurologist or psychiatrist experienced in treating TS. You must have had trials of drugs from three different classes of drugs that have not worked

for you. Study staff will discuss this with you.

f. You must have received stable and effective treatment of any other existing medical or psychological problems for the past 6 months.
g. Your current TS related-medication(s) must be stable for at least a month without a dose change prior to surgery and you must be willing to keep these medications stable and unchanged throughout the study or you must be off of TS-related medications for at least three months prior to surgery.
h. If your tics involve only one group of muscles or might be controllable by botulinum toxin treatment, you must try botulinum treatment before considering surgery.
i. You must have a negative urine drug screen for illegal substances not to include marijuana/cannabinoid use.
j. You must give informed consent.

You cannot participate in this study if:

a. You have unexplained gaps in your medical history
b. You have a simple motor tic or movement disorder other than TS, or medication-related movement disorders from TS medications.
c. You have had any previous brain surgery including deep brain stimulation, ablative capsulotomy or cingulotomy (the surgical cutting of a specific part of the brain for the purposes of providing treatment).
d. You have another psychiatric condition (including body dysmorphic disorder, a delusional disorder or a biological brain disorder), dementia or cognitive dysfunction that would place you at risk for worsening cognition and/or may impact your ability to comply with study procedures. Also included is any other psychiatric disorder that requires medications or treatments that would interfere with the functioning of the DBS device.
e. You have any significant substance abuse or dependence (e.g., stimulants, alcohol, opiates, benzodiazepines) within the past six months.
f. You have a severe medical disease including cardiovascular disorder, lung disorder, kidney disease, chronic neurological disease, hematological disease, or frailty that impacts tolerability of the surgery as judged by the screening physicians.
g. Your pre-surgery MRI is considered abnormal. You may also be excluded if your brain is considered very small as there may be an increased risk for bleeding.
h. You have a history of serious suicidal behavior, are unable to control suicide attempts, or are currently at risk of suicide, in the judgment of the investigator.
i. You have head-banging tics or tics that have the potential to damage the DBS System.
j. You are currently pregnant or breast-feeding, plan to become pregnant during the study, or are not using effective contraception (See section 10 of this form for appropriate methods.)
k. You are currently enrolled in another investigational study.
l. You have an implant such as a pacemaker or neurostimulator containing

electrical circuitry or that generates electrical signals.

m. You have any metal orthopedic pins or plates, metal orthodontics, or non-removable body jewelry.
n. You require diathermy treatments during physical or occupational therapy.
o. You have a problem that will require repeat Magnetic Resonance Imaging (MRI) scans. MRI has not been evaluated for safety with the RC+S system, so participating in this study will preclude future MRIs as long as the device is implanted.

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.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

Normal clinical care for TS includes cognitive behavior therapy, medication, supportive psychotherapy, and/or a combination of the two. To meet entry criteria for this study, you must have already tried these methods and they did not help your symptoms. DBS is considered experimental for the treatment of TS and would not be done as normal clinical care.

7. What will be done only because you are in this research study?

Screening Visit(s): If you decide to participate, this visit may take up to 6 hours and you will be asked to read, sign, and date this informed consent before any study-related procedures are performed. In order to find out if you meet the requirements to participate in the study, you will be evaluated by study doctors and members of the research staff. During this time you will be asked a series of questions by interview, questionnaires, and checklists about your symptoms. If you become uncomfortable, overly anxious or sad as a result of being asked any items on the questionnaires, at any of the visits, you can choose to stop. If the assessor feels it is necessary, he or she can recommend appropriate treatment. The screening evaluation will include questioning regarding your sexual behavior and drug use. The evaluation will also involve collecting basic information (such as age, sex, race) and psychiatric, medical, and family history. The questionnaires and checklists are listed below. You will also have a physical and neurological exam that will include measuring vital signs (heart rate and blood pressure), and collecting urine samples for routine testing. If you are a woman of child-bearing potential, a test for pregnancy will be performed. The urine sample will also be tested for illegal drug use.

- Yale Global Tic Rating Scale (YGTSS) and Modified Rush Tic Rating Scale (MRTRS) - this evaluates your current level of tics.
- The SF-36® Health Survey and Quality of Life Assessment Schedule (QOLAS) are forms that measure quality of life and will be completed by you.
- Hamilton Rating Scale for Depression (HAM-D) and Beck Depression Inventory II (BDI) – these evaluate your current level of depression.
- Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) – this evaluates your level of obsessions and compulsions.
- Young Mania Rating Scale (YMRS) - evaluates the presence and level of mania.
- Columbia Suicide Severity Rating Scale (CSSRS)- this evaluates the presence of suicidal ideation or behavior.
- Quality of Life Assessment Schedule (QOLAS)-assesses quality of life in 5 domains
- The Conner's Attention Deficit Questionnaire
- Premonitory Urge for Tics Scale (PUTS)- assesses intensity of urge to tic
- You will be interviewed and other information about your medical condition documented.

You will be asked to complete these questionnaires and checklists at this screening visit and throughout your participation in this study. You and the study doctor or coordinator will be videotaped (including sound) while you are completing some of these questionnaires throughout the study (particularly the YGTSS and MRTRS, which evaluate current tics). These sessions are videotaped so they can be reviewed and/or scored by a doctor who is not involved in your treatment at baseline and approximately 6 months post-surgery. The videotapes will be used for study purposes. Videotapes will continue to be used to compare subject data after the study is closed. Also, with your permission, videos may be used to teach others about the pre-surgery and post-surgery differences in tics.

You will also have detailed neuropsychological testing, including tests of perception, learning, and memory. For those tests you will use paper and pencil or a computer. These evaluations include: the Weschler abbreviated scale of intelligence (WASI-II), digit span and spatial span, California Verbal Learning Subtest, Story ("Logical Memory") and Face ("Visual Reproductions") Memory Subtests of Wechsler Memory Scale-WMS-III, Judgment of Line Orientation, Stroop Test, Trailmaking Test, Word Fluency Test, Grooved Pegboard, and mood measures to evaluate how your mood is being affected by the DBS treatment (Beck Depression Inventory-2 and State Trait Anxiety Inventory). You can choose to discontinue taking any of these assessments or tests at any time. If you decline to be videotaped, you will not be able to participate in the study.

You will also meet with the neurosurgeon. This visit will give you a chance to ask any questions you may have about the surgery. The neurosurgeon will take a brief medical history and perform a brief physical exam. He will also review any brain imaging you have in your medical record, and will tell you about the surgical procedure. He will then discuss the risks and benefits of surgery and answer any

additional questions you may have.

The research team will also review any other neurological scans you may have had in the past.

Any other procedures you had done previously, along with the results of our screening will be reviewed by a multi-disciplinary DBS panel (neurologist, neurosurgeon, neuropsychologist, psychiatrist). They will make sure that all other options for treatment have been explored. They will also make sure you have an accurate diagnosis of severe TS with no other treatment options. The panel must unanimously agree that you meet all inclusion/exclusion criteria and are a suitable candidate for surgery.

Baseline Visit: This visit is expected to take up to 4 hours. If you are recommended for participation by the panel, you will be asked to try to stay on the same medication or medications you are taking now throughout the study; unless you, the investigators, and your personal psychiatrist agree that your medication needs to be changed.

At this time, your entry criteria will be reviewed and you will be asked to complete some of the questionnaires discussed earlier.

Surgery: It is extremely important that your head does not move during the surgery. To accomplish this, the morning of your surgery a metal frame called a stereotactic headring will be attached to your head under local anesthesia. It will be attached to your skull using plastic and aluminum set pins. You will feel a lot of pressure as the headring is attached. The headring is a special instrument that allows the neurosurgeon to find the correct path to where he needs to place the DBS and superficial leads in and on your brain. Next, a CT (cerebral computerized tomography) scan will be performed. The pre-surgery MRI scan is then fused on to the CT scan so we can determine the exact area(s) in your brain where the leads will be placed.

After you have been prepared for the surgical portion of the procedure, a member of the surgical team will inject local anesthetic in your scalp and begin the procedure. An opening will be made in your scalp and two openings will be made in your skull for placing the deep DBS leads, and two opening will also be made to place the superficial DBS leads that will be placed on top of your brain covering. In summary you have two small holes on each side of the skull. The exact shape of the opening will be made to fit the DBS lead. The DBS will be placed in the skull behind and above your ears. Two small openings, each about the size of a nickel, will be made in your skull for putting in the DBS leads. Each lead will be placed deep within your brain tissue and will be connected to an pacemaker in your chest. The majority of the surgical procedure will be done under local anesthetic, meaning you will be awake but you should not feel any pain. However, you will need to be put under general anesthetic to implant the pacemakers. With general anesthesia, you will be given one or more drugs that make you sleep and not feel pain during the surgery. The leads and pacemaker battery will all be implanted within 30 days in two settings (one for the leads, one for the pacemaker battery) .

Each pacemaker battery is labeled to last 9 years before it needs to be replaced. The surgery to replace a battery is not as major as the original surgery to implant the DBS System. A small opening is made in the chest over the battery so that it can be disconnected from the leads and be removed. Once the new battery is put in place, the leads are then connected and the opening in the chest is closed. Your replacement battery could be the Summit RC+S, or the commercially available RC device. In the latter case, the superficial leads placed on top of your brain will be left in place disconnected, with the thin end of the extension exposed and buried deep to the replacement battery. This will avoid the risk of inadvertent delivery of unintended stimulation from the leads placed on top of your brain as a potential programming error. Only continuous (conventional) DBS can be delivered from the RC devices.

Postoperative Procedures/Evaluations: You will probably stay in the hospital for a couple of days after lead implantation surgery. The pacemaker battery is an outpatient surgery. At that surgery, the pacemaker will be turned ON to sense and record brain activity, but not to deliver any stimulation. Using a hand-held wand, recorded information from the pacemaker will be streamed.

You will also be given a remote control that can be used to turn off the pacemaker at any time in case you feel discomfort from the stimulation. You will be given a Remote control User Guide that explains the use and care of the magnets.

After the IPG implant, you will be scheduled to return in approximately one week to activate your pacemaker. We will wait approximately 30 days after lead implant before activating your pacemaker in order to make sure that the swelling has gone down and that the site where the pacemaker was implanted has healed. We feel that 30 days are needed for the sites to heal, allowing your body to adjust to having the stimulator implanted and to be ready so that it is safe to have the stimulator turned on.

During the pacemaker implant visit, a post-implant CT scan will be performed. You will have a threshold visit approximately one week following the pacemaker implant (+/- 7 days) where your pacemaker is set and turned on, and then you will return to the clinic for routine programming visits once a month (+/- 14 days) until month 6 post-operatively, up to 12 months (+/- 14 days) past your first programming visit, if your settings have not been fully optimized as judged by the investigator. During each visit starting with Month 1, physiology data collection will be performed, which may take about 3-5 hours to 3-5 full days depending on the complexity of your individual case. You will be allowed breaks as often as needed. For this portion, you will be asked to put on several body sensors, and neurological signals will be streamed into a laptop. The signals from your deep brain stimulation device will also be streamed. This information will be used to inform programming settings for future visits that are tailored to your individual case.

You will be asked to come in about 180 days (6 months (+/- 14 days)) after your surgery for another full battery of motor tests and a psychiatric assessment. This is the end visit for the first part of the trial. This visit will be postponed if the investigator

believes your stimulation settings have not been optimized. Additional assessments will be repeated every 6 months (+/- 14 days) after this end visit, for at least the next 2 years. The neuropsychological tests will be repeated only at 12 months (+/- 14 days). During these check-up visits the effectiveness and functioning of your stimulators will be checked. You will also be asked to come in for physical exams yearly to monitor your health. A schedule of assessments is below:

VISIT	MINI	YGTSS	MRTRS	SF-36	HAM-D	Y-BOCS	QOL AS	YMRS/ CAARS	Neuro-psychology Battery	C-SSRS
Pre-operative	X	X	X	X	X	X	X	X	X	X
Month 1 (day 30)*		X	X	X						X
Month 2 (day 60)**		X	X	X						X
Month 3 (day 90)**		X	X	X						X
Month 4 (day 120)**		X	X	X						X
Month 5 (day 150)**		X	X	X						X
Month 6 (day 180)**		X	X	X	X	X	X	X		X
Month 12 **		X	X	X	X	X	X	X	X	X
Month 18 **		X	X	X	X	X	X	X		X
Month 24 **		X	X	X	X	X	X	X		X
Followup visits (2-4 visits within a 12 month period)		X	X							X
Visits 6.1-6.4***		X	X							X

*+/- 7 days, **+/- 14 days, *** Visits 6.1-6.4 will be up to one month at a time (+/- 14 days), for up to 4 months, at a time point approved by the Principal Investigator between Month 6 and Month 36, based on the individual's response to acute responsive stimulation. If they occur beyond month 24, they make take the place of the follow up visits.

At the 6 month visit or later, we will test a responsive stimulation setting on the device and after this visit you will be able to choose the setting that you like the best for chronic treatment (continuous stimulation or responsive stimulation). If you respond favorably (have good effects with few side effects) during this testing at the visit, we will test chronic responsive stimulation for one month at a time (+/- 14 days). This will occur at an Investigator-approved time point between Month 6 and Month 36. You will be given a patient programmer, which will allow you to turn off responsive stimulation and switch back to your previous standard continuous therapy as desired. However, if we are not able to pinpoint brain activity that predicts your tics, we will not be able to perform a responsive setting.

At the end of the initial 24-month study period, you will have the choice of 1) continuing active stimulation at current settings, 2) continuing active stimulation but

searching for new settings, 3) discontinuing stimulation, and 4) discontinuing stimulation and removing the device. If you continue to receive active stimulation at the conclusion of the study, you will be followed by the PI and be seen at yearly intervals. There will be a 12 month follow-up period to allow for continued programming and physiology collection, for total of 36 months. Follow-up visits during this 12-month period will include device programming and physiology data collection. Because the RC+S devices can only be programmed using a unique research programmer, we will provide routine standard care (annual programming visits) for the duration of battery life (labeled to last 9 years), even beyond the 36 month study period. These visits will be treated as standard neurology visits at our clinic, as opposed to research visits. At any time during the study or follow-up period, you may request to come to the clinic for an "unscheduled visit." Assessments performed at such visits will depend on the reason for the visit and will be at the discretion of the investigator. Screening interview, diagnostic & medical evaluations, physical exams, vital signs, collecting urine samples for pregnancy test (if applicable) and urine drug screen, study assessments, and Neuropsychological Battery are done only because you are in this study. The DBS surgery is considered experimental for the treatment of TS and is done only because you are in this research study. The MRI scan and CT scan are required for DBS surgery. All visits will be performed at the University of Florida, with the exception of post-Month 12 visits. As needed, data collection and programming past month 12 (including visits 6.1-6.4 if they occur after Month 12) may be performed in your home. Please discuss with your study doctor for details. The time and procedures involved will be identical regardless of location. Throughout the duration of the study, you are responsible for keeping the device charged as needed.

On occasion, you may be asked to stream the data streamed from your brain to an external tablet in your home (after undergoing training), using a bluetooth device that may be stored in your pocket. You may also be requested to make brief video recordings of your tics, using the external home tablet. This combined data will be used to improve the efficiency and quality of your personal stimulation, by providing real-time feedback of how your brain data is interacting with the closed-loop device. This information will be uploaded in a HIPAA-secured cloud site for rapid access by investigators. With your permission, investigators may make home visits to assist with or troubleshoot data streaming and wearable monitors. Prior to home testing, you will be instructed on how to exit adaptive mode of your device at any time and return to open-loop mode should discomfort occur, but you are encouraged to consult with study staff if possible prior to doing so.

If your RC+S battery is depleted during the course of the study, it may be replaced with another RC+S battery, or the commercially available RC device (also rechargeable). However, only the RC+S battery allows for closed loop stimulation, so if you receive the RC device, you will be transitioned to chronic stimulation and seen yearly as per DBS standard of care once the 36-month study period ends. If you have your battery replaced with another RC+S battery, you will be seen here at our clinic through the duration of the battery life (labeled to last 9 years) since the

research programmer is limited in availability.

If you have any questions now or at any time during the study, please contact Dr. Okun listed in question 3 of this form.

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative

If you have any questions now or at any time during the study, please contact one of the research team members listed in question 3 of this form.

8. How long will you be in this research study?

We expect your participation will last at least 36 months (24 month initial study period, followed by a 12 month followup period) At the end of this initial 24 month study period you will have the choice of continuing or discontinuing stimulation. There will be a 12 month followup period to allow for continued programming and physiology collection, with a minimum of 2 and a maximum of 4 visits, for total of 36 months. Because the RC+S devices can only be programmed using a unique research programmer, you will continue to be seen at our clinic for routine standard care (annual programming visits) for the duration of battery life (labeled to last 9 years), even beyond the 36 month study period. These visits will be treated as standard neurology visits at our clinic.

9. How many people are expected to take part in this research study?

We expect to consent and screen 60 individuals in order to enroll ten.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

10. What are the possible discomforts and risks from taking part in this research study?

The implantation of a pacemaker requires major surgery and you will experience pain and discomfort during the post-surgical recovery period. The possible risks to you as a participant include, but are not limited to, the potential risks outlined below. You will also be given the Medtronic Patient Manual. It is important that you read it and discuss any questions and concerns with your study doctor and/or staff. In particular, you should be aware that you might experience a worsening of symptoms.

Subjects will be monitored throughout the study for the presence of suicidal ideation or behavior using the Columbia Suicide Severity Rating scale (C-SSRS) at each visit.

If any side effects or any other signs or symptoms develop after the surgery you should report them to Kelly Foote, M.D. Dr. Foote is the neurosurgeon involved in implanting the wires and stimulators and can be reached at 352-273-9000 from 8:30 a.m. to 5:00 p.m. weekdays. Dr. Foote can be paged at 877-364-1431 at any time.

Possible risks of surgical implantation of the device:

Possible risks associated with your DBS surgery:

1. Bleeding or fluid inside of the brain, on the surface of the brain, or in the space between the skull and brain during your surgery that could result in change in consciousness, paralysis (not being able to move), stroke, or death.
2. Cerebrospinal Fluid (CSF) leakage during your surgery could result in a dull or throbbing headache or need for additional surgery.
3. There is the possibility of complications, injury and even death from all forms of surgical anesthesia.
4. Meningitis, encephalitis, or brain abscess resulting from infection involving the brain and/or central nervous system
5. Swelling of a small part of the brain around the DBS lead
6. Bleeding into the brain or stroke-like conditions resulting in temporary or permanent injury to the nervous system, or death; these could occur at any time after the DBS leads are placed
7. Non-infected cyst of the brain around the end of the DBS lead

Possible risks immediately after your DBS surgery:

1. CSF leakage after your surgery could occur and might result in a dull or throbbing headache or need for additional surgery.
2. Short-term pain in the head and neck might occur.
3. Infection could occur after surgery, including meningitis (an infection that causes swelling of the lining around the brain and the spinal cord and which has the potential to cause brain damage or hearing loss).
4. Allergic reaction to the implanted parts is possible but rare.
5. Discomfort or lack of healing of the skin area could occur at or around the site of the implanted parts.
6. Surgery could cause swelling under the skin of the scalp or a mass of clotted blood inside or on the surface of the brain or in the space between the skull and brain that may apply pressure to the brain.

Possible risks with the DBS system:

1. Although pain and negative changes in mood during stimulation could occur, test stimulation is performed to determine stimulation settings that do not

cause pain, discomfort, or negative changes in mood.

2. Pain or discomfort that lasts a long time and/or additional sensitivity may occur where the implanted parts were placed.
3. Movement of the lead from where it should be in the brain or loose electrical connections could cause therapy to stop working, could cause pain, or possibly cause a sensation of pricking, tingling, or creeping on the skin.
4. Stimulation has the potential to cause a seizure and there is a possibility that this could bring about a seizure disorder.
5. Certain therapy settings may cause involuntary movements (i.e., eyelid blinking, twitching). These movements usually go away after the therapy settings have been adjusted.
6. Changes in your brain cells or reduced sensitivity of your brain to stimulation could cause therapy to stop working.
7. The effects of long-term brain stimulation are not completely known and there could be some risk of brain tissue damage.
8. The battery is labeled to last 9 years after implant, depending on use. However, frequent and/or high current stimulation may shorten the "life" of the battery. When the battery runs out, an additional surgery for replacement will be required if you or your study doctor still want the device to work. The risks for this procedure are expected to be lower than those of the first implant since the replacement surgery does not involve cutting into bone or placement of leads in the brain.
9. You are required to charge your device as often as needed to maintain its functionality. This could be as often as daily. Failure to properly recharge the stimulator will result in loss of stimulation. You will receive training on how to recharge your device. You will receive written instructions to take home with you, and you can reach the research team if you encounter any issues.
10. As with any electronic device, the DBS System may not work. A system malfunction may be because the battery is running low or is out of energy. It could also be because of an electrical short, open circuits, lead fractures, or lead insulation failures, or damage as a result of head trauma. These malfunctions are unpredictable, and may result in too little stimulation. A malfunctioning pacemaker may require minor surgery to replace. Although the pacemaker is designed to turn off if over stimulation or excess current occurs there is a possibility that product failure could result in brain tissue damage.

Other Possible Risks Associated with this Study:

1. The device may be discontinued and thereby unavailable to patients for replacements due to damage or battery depletion. The device can be removed or left implanted until the battery runs out. Device removal (explantation) will be paid for by subject's private insurance and/or Medicare or CMS. Device explantation may involve the removal of the battery in your chest, while your DBS electrodes could be left in place. You may also choose to have the DBS electrodes removed as well. One publication by Liu and

colleagues published in the Journal of Neurosurgery in 2012 reported 12.8% chance of bleeding within the skull when DBS electrodes were removed. These bleeds were detected by postoperative CT scans. However, they were reported to be asymptomatic.

2. Worsening of TS and other psychiatric symptoms, such as those associated with mania, could possibly occur and might require medical treatment.
3. You might experience, or have a worsening of, suicidal thoughts or impulses.
4. Replacing or permanently removing any or all implantable parts may be medically necessary. The implanted parts may cause fibrosis (a "build-up" of scar tissue) that could get in the way or stop their removal. With any surgery involving removal of such parts, there is a risk of intracranial bleeding (bleeding inside the brain).
5. The following risks have been reported with the use of systems that provide chronic (constant) stimulation to deep brain structures. These reported risks may be related to areas of your brain that will be stimulated.
    a. In a study of 160 people treated for Parkinson's disease with another deep brain stimulator (DBS), serious side effects included bleeding in the brain (7.5%), infection related to the deep brain stimulator (10.6%), weakness or loss of energy (10%), and weakness or paralysis affecting one side of the body (8.1%). There were ongoing serious side effects related to the stimulation in 3.1% of the patients, including pain, problems with speech, and worsening of the Parkinson's disease symptoms. Serious on-going side effects related to the device occurred in 6.3% of the patients and included problems with the DBS system, infection, skin breakdown in the area where the device was implanted, and worsening of Parkinson's disease symptoms.
    b. In another study of 424 patients with tremor who were implanted with the same deep brain stimulator used for the patients with Parkinson's Disease, side effects related to the surgery to implant the device included pain (6.6%), bleeding in the brain (3.1 %), infection (2.6%), skin breakdown in the area of the device (1.9%) and a change in skin sensation (1.4%). Side effects related to brain stimulation included a change in skin sensation (33%), difficulty saying words (9%), difficulty with balance (5%), and weakness (5%). Most of these side effects were tolerable and did not require any change in the treatment.
6. While the following potential risks have not been reported with the use of the DBS System, they have been reported with systems that provide chronic (constant) stimulation to deep brain structures. These reported risks may be related to the area being stimulated, and include:

    Abnormal dreams, thinking and vision; amnesia (not being able to remember); apathy (disinterest in others and events); chest pain; delusions (thinking things that are not true or real); encephalopathy (slowing of thoughts); deep thrombophlebitis (deep blood clots); difficulty breathing, swallowing and walking; dizziness; drowsiness; dysesthesia (pain or uncomfortable sensations after being touched by ordinary things); fainting; hallucination (seeing or hearing things that are not real);

hostility; increased salivation; paresthesia (abnormal burning or prickling sensation); paresis/paralysis (not being able to move part or all of your body); pneumonia; postural hypotension (dizziness upon standing); rapid heart rate; speech disorders/difficulty speaking; vomiting/nausea.

7. The Summit programmer is unique to the device under study. Commercially available programmers do not support the Summit system. Therefore, following your participation in the study, you will be limited in clinical programming follow-up to the University of Florida.
8. While the following potential risks have not been reported with the use of the DBS System, they have been reported with systems that provide stimulation to deep brain structures in an acute (short-term) environment, like in the doctor's office. These reported risks include all those risk listed above as well as:

   Changes in cognitive function; changes in movement, standing or walking; changes in smell/taste; encephalopathy; gastrointestinal symptoms; increased depression or worsening of depressive symptoms; memory experiences.

Possible risks associated with other medical procedures and devices:

The Summit RC+S system has not been evaluated for MRI safety. Hence, it is important for you to consider the fact that you would not be able to undergo any MRI scans in the future. MRI are well suited to image the non-bony parts or soft tissues of the body. MRI may help diagnose or monitor treatment for conditions such as tumors of the chest, abdomen or pelvis; disease of the liver, bile ducts or pancreas; inflammatory bowel disease; heart problems; malformations or inflammations of the vessels. If an MRI is needed, it is important for you to contact your doctor for advice on alternative imaging that is safe.

Electromagnetic Interference (EMI) is electrical or magnetic energy that is strong enough to interfere with the function of your pacemaker. This may cause the pacemaker to not deliver stimulation for minutes to hours. Experience with the DBS System to date suggests that EMI has not compromised device performance or safety. While it is extremely unlikely to happen, there is a possibility that the DBS settings could change because of EMI.

Diathermy, a treatment that uses high-frequency electromagnetic radiation, electric currents, or ultrasonic waves to produce heat in body tissues, should not be applied anywhere on the body even if your pacemaker is turned OFF. Energy from shortwave or microwave treatments can be sent through the implanted brain stimulation system and can cause permanent brain damage which may cause severe injury, coma, or death. This not caused by a device malfunction. Rather, it is caused by the interaction of two devices (neurostimulation system and diathermy machine) when they are working properly. This warning does not apply to microwave ovens. Microwave ovens are safe to use and will not interfere with the pacemaker.

You absolutely CANNOT be treated with any type of short wave or microwave diathermy device whether or not it is used to produce heat. Both heat producing and non-heat producing treatments and diagnostic tests involving the use of sound, vibration, or electromagnetic (such as shortwave or microwave) energy are used by a variety of health care professionals, such as physical therapists, occupational therapists, chiropractors, physicians, dentists, sports therapists, ophthalmologists (eye doctors) and others. Because some of these treatments and diagnostic tests could interfere with or damage the DBS or pacemaker, *please advise all of your health care professionals that you should not be exposed to diathermy treatment.*

You CANNOT receive therapeutic ultrasound treatment to your head or neck. Energy like this may be sent through your implanted brain leads resulting in brain damage. You should avoid therapeutic ultrasound treatment below the head or neck unless the risks of not using the treatment outweigh the risks of using it. The effects on the DBS System of the energy made from therapeutic ultrasound treatments below the head or neck are not known. Diagnostic ultrasound to any part of the body is safe and will not interfere with the DBS System.

Lithotripsy (the crushing of stones, usually in the gallbladder or urinary tract, using shock waves) should be avoided unless the risks of not using the treatment outweigh the risks of using it. If lithotripsy therapy is required, avoid directing the lithotripter (the device used to crush the stones) at the head. Energy delivered to the head may damage the DBS System. This could result in loss of therapy, and additional surgery to remove or replace parts of the DBS System.

Radiation therapy (usually for cancer) anywhere on the body should be avoided unless the risks of not using the treatment outweigh the risks of using it.

Electrocautery (using electrical current to stop bleeding during surgery) applied near the pacemaker may cause it to turn off and temporarily stop delivering therapy until it is reprogrammed by your doctor. Electrocautery applied directly to the pacemaker or leads may send energy through your implanted brain Leads resulting in brain tissue damage. If electrocautery is required, keep the electrical current as far away from the pacemaker and leads as possible. Use of bipolar electrocautery is recommended.

Other medical procedures such as dental work, electrolysis, or the implant of another medical device in the body may be performed with caution. Talk to the study doctor before such procedures.

Your pacemaker may interact with other active medical devices (such as pacemakers and defibrillators) implanted in you. Talk to the study doctor about any such medical devices you may have currently implanted.

Possible risks associated with other equipment:

Magnets that are contained in such products as stereo speakers and power tools, as well as those used as a remedy for other ailments, should be kept at least 4

inches away from the pacemaker implanted in your head. The pacemaker may not deliver stimulation while these magnets are closer than 4 inches from the pacemaker or for minutes to hours after removing the magnets. Most headsets and earphones available in stores will not interfere with the pacemaker, but not all have been tested.

It is possible that security screening devices (such as theft detectors, airport security systems, etc.) may stop stimulation by the pacemaker for minutes to hours.

Risks associate with explantation:

If your doctor determines that it is necessary to move the device, or if you request that the device be removed, you have the option of removing the battery and leaving the electrodes in place or removing the battery and the electrodes. One publication by Liu and colleagues published in the Journal of Neurosurgery in 2012 reported 12.8% chance of bleeding within the skull when DBS electrodes were removed. These bleeds were detected by postoperative CT scans; however, they were reported to be asymptomatic. Explantation surgeries will be paid for by subject's private insurance and/or Medicare or CMS

Other possible risks:

You may feel minor discomfort during a complete neurological and psychiatric evaluation. Sometimes people may feel uncomfortable talking about sensitive topics. The research team will take every precaution to make sure you are comfortable talking about these kinds of subjects.

You may experience mild discomfort resulting from answering the questionnaires and checklists and discussing potentially difficult topics. However, most people welcome the opportunity to discuss their experiences with a trained clinician.

The psychological tests that will be administered at different times during this study are either computer or paper and pencil tests. None of the tests poses any significant risk, although some people may find the testing tedious or even frustrating. The testing can last up to 8 hours, spread over two days. Breaks are included during the testing to make it easier to complete.

The risks of CT scans are relatively minor. The risks of MRI scans prior to implant of the DBS System are relatively minor. The MRI scanner produces a "hammering" noise that has been reported to produce hearing loss in a very small number of participants. You will be provided with earplugs to reduce this risk. You will be receiving a CT and MRI scan before the DBS procedure.

You may experience discomfort when inside the scanning equipment. The inside of both the CT scanner and the MRI scanner are confined. You will be closely monitored and repeatedly checked on by the research team to insure that you are as comfortable as possible. You will be in constant contact with the research team via a radio system and a distress button. Your time spent in the scanner when the magnets are active will be limited to what is absolutely necessary. Sometimes people feel uneasy because they are being restrained. If this happens you can tell the research team of you are

uncomfortable and discontinue the scan.

This research study involves exposure to radiation from brain CT scan. The total amount of radiation that you will receive from one of these studies is about 210 millirems, and is approximately equivalent to a whole body exposure of 8 months of natural background radiation.

The radiation exposure in this study is thought to be minor. However, the effects of radiation exposure add up over your lifetime. Repeated exposures may increase your risk of injury or disease. When deciding to enter this study you should consider previous and future potential exposures. The investigator can provide you with a contact person if you would like more information about radiation exposure.

Although this procedure is designed to control your TS symptoms, it is an unproven therapy and experience with it is limited. Therefore the possibility exists that stimulation could have no effect on your symptoms or even make them worse. It is possible that you may have side effects when the stimulation comes on, including tingling or uncomfortable sensations on the face or body, perceiving unusual tastes or smells, or experiencing weakness, unsteadiness, dizziness, fainting, or possibly seizures. Other possible side effects of stimulation are trouble speaking, or changes in mood, memory (including a memory flashback to past events), thinking and energy level. It is also possible that the combination of the stimulation and your medication might result in more side effects than you would have from either treatment alone. Medication treatment will continue during the study, since we believe that the chance of your TS symptoms improving is better if stimulation is added to your ongoing medication and behavior therapies.

As discussed above, if stimulation improves your TS symptoms, mood or anxiety during this trial, it is possible that these symptoms may worsen if the stimulation stops, especially if the stimulation stops suddenly. That could happen when the battery becomes depleted, or if the pacemaker is inadvertently shut off, as discussed in the section right below. This worsening might take the form of worsened TS, anxiety or symptoms of depression including low energy, motivation, sadness and even suicidal thinking. If any such symptom worsening occurs during this study, whether or not you believe that the stimulation has changed, you should immediately notify your study doctor.

We cannot predict whether brain electrical stimulation for TS that has not responded to other available treatments will be effective for you as an individual. We cannot guarantee you will receive any benefits from this study. As noted above, there is the possibility that your symptoms might worsen as a result of stimulation.

The safety and effectiveness of the DBS System has not been studied in pregnant women. Therefore, women of childbearing potential must use an acceptable method of birth control while in this study. This includes women in perimenopause/early menopause, but who have not achieved two years without a period. Birth control for the purposes of this study is: hormonal contraceptives ("the pill", Depo-Provera injections); intrauterine devices (IUDs); double barrier method of contraception

(condom plus spermicide, condom plus diaphragm, etc.). If you become or suspect that you are pregnant during the study, you must notify the study doctor immediately. You and your doctor will discuss the risks versus benefits of continued stimulation. If you become pregnant after you have enrolled in this study but before your implant surgery, you must withdraw from the study due to the risks of general anesthesia to a developing fetus.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 18-22 in this form discuss what information about you will be collected, used, protected, and shared.

This study may include risks that are unknown at this time.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform Dr. Okun (listed in question 3 of this consent form) or the person reviewing this consent with you before enrolling in this or any other research study or project.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call the PI or contact person listed on the front page of this form.

11a. What are the potential benefits to you for taking part in this research study?

You may or may not personally benefit from participating in this study. There is a possibility that you will have improvement in your TS symptoms

11b. How could others possibly benefit from this study?

The information obtained from this study may help improve the treatment of severe TS in the future.

11c. How could the researchers benefit from this study?

Dr. Okun may benefit if the results of this study are presented at scientific meetings or in scientific journals.

12. What other choices do you have if you do not want to be in this study?

Although you meet criteria for brain surgery such as DBS, it does not mean brain surgery is the only option remaining for you. You may elect to seek current

treatments for your Tourette syndrome and associated co-morbid conditions, including both pharmacological and psychological interventions. Sometimes people with TS who have had severe illness for many years will show improvement with a particular combination of medications. Dr. Okun will be glad to discuss these with you. When considering participating in this study, you will need to carefully weigh the pros and cons, the potential benefits and the potential risks. Remember that there may be other options.

13a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled. The Summit programmer is unique to the device under study. Commercially available programmers do not support the Summit system. Therefore, if you decide to discontinue the study, you will be limited in clinical programming follow-up to institutions (such as UF) who have the Summit programmer. The Principal Investigator will continue your care with routine annual programming visits, as per standard of care, throughout the lifetime of the battery (labeled to last for 9 years) due to the limited availability of the research programmer. These visits will be billed to you or your insurance company.

If you decide to withdraw your consent to participate in this study for any reason, please contact the research team member listed in question 3 of this form. He will tell you how to stop your participation safely.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office at (352) 846-1494.

13b. If you withdraw, can information about you still be used and/or collected?

If you withdraw from the study, information that has been collected to that point will be used in the analysis of data.

13c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- The sensing function of your device fails but you are still receiving symptom benefit. In this case, you would be withdrawn from the study and be followed in clinic for standard device programming.
- You do not qualify to be in the study because you do not meet the study requirements. Ask the Principal Investigator if you would like more information about this.
- You need a medical treatment not allowed in this study.
- The investigator decides that continuing in the study would be harmful to you.

- Study treatments adversely affect your quality of life by making your symptoms worse.
- You become pregnant, and the study treatment could be harmful to the baby.
- The study is cancelled by the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and/or other administrative reasons.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

14. If you choose to take part in this research study, will it cost you anything?

Study Devices

The SUMMIT RC+S device, will be provided at no cost to you while you are participating in this study. However, the cost of the battery replacements will be billed to you or your insurance company. You will be responsible for paying any deductible, co-insurance, or co-payments for these services, and for any non-covered or out-of-network services.

Study Services

The Sponsor will pay for the following study-required services at no cost to you:

1. Office visits and physical exams required by the study.
2. Study questionnaires
3. Neuropsychological Testing
4. Neurosurgeon Office Visits
5. Psychiatric Assessments
6. Review of Medical history and Inclusion/Exclusion Criteria
7. Study required labs
8. DBS Implantation surgery
9. Postoperative Procedures/Evaluations
10. Study-only urine pregnancy test.
11. Study-only urine drug test.
12. Study only MRIs and CT scans

If you receive a bill for these services, please contact Michael S. Okun, MD at (352) 273-5550 or Cami Swartz at (352) 733-2429.

Items/Services Not Paid for by the Sponsor

Any other medical services provided to you that are not directly required by this study will be billed to you or your insurance company in the usual manner.

Replacement Procedures

Battery replacement and replacement procedure(s) will be billed to you or your insurance company. You will be responsible for paying any deductible, co-insurance, or co-payments for the replacement procedures, and for any non-covered or out of network services.

Device Explant

If your study doctor determines it is necessary to remove the device, or if you request that the device be removed, the cost of removal will be billed to you or your insurance company.

You will be responsible for paying any deductible, co-insurance, or co-payments for these explant services, and for any non-covered or out-of-network services.

Some insurance companies may not cover costs associated with studies. Please contact your insurance company for additional information.

15. Will you be paid for taking part in this study?

You will receive a $200 stipend to help compensate you for your time and travel. This will be payable on a prepaid Visa card at the conclusion of each study visit, except the post implant visit (as it does not require a separate trip to the study site). One unscheduled visit will be compensated ($200) per calendar year, though you may request as many as needed. Any unscheduled visits requested by the study team will be compensated ($200).

16. What if you are injured because of the study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence. .Please contact Dr. Michael Okun at (352) 273-5550 if you experience

an injury or have questions about any discomforts that you experience while participating in this study.

17. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Complete past medical and psychiatric history to determine eligibility criteria
- Records of past physical exams, treatments, evaluations, and any other procedures you may have done in terms of TS only
- Physical exam, laboratory, MRI, and other test results
- Psychiatric and neurological assessments, in the form of interviews and questionnaires
- Information related to diagnosis and treatment of a mental health condition
- Records about study devices
- Social security number
- Telephone number
- E-mail address

This information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

18. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

- to determine the effectiveness of the study device in treating TS

Once this information is collected, it becomes part of the research record for this study.

19. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows. These people include the:

- the study Principal Investigator listed in question 3 of this form and research staff associated with this project.
- other professionals at the University of Florida or Shands Hospital that provide study-related treatment or procedures.
- the University of Florida Institutional Review Board (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research).

20. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- the study sponsors listed in Question 4 of this form.
- United States and agencies responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections
- Medtronic, the maker of the device
- Your insurance company for purposes of obtaining payment.

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

21. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others as described above throughout your participation in the study. Once you complete the study, your protected health information will be anonymized (that is, all identifying links between you and your information will be removed), used, shared with others and maintained in a secure database indefinitely.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

Consent to be Videotaped and to Different Uses of the Videotape(s)

With your permission, you will be videotaped during this research. Your name or personal information will not be recorded on the videotape, and confidentiality will be strictly maintained. When these videotapes are shown, however, others may be able to recognize you.

The Principal Investigator of this study, _____, or *[his/her]* successor, will keep the videotape(s) in a locked cabinet. These videotapes will be shown under *[his/her]* direction to students, researchers, doctors, or other professionals and persons.

Please sign ***one*** of the following statements that indicates under what conditions Dr. _____ has your permission to use the videotape.

I give my permission to be videotaped solely for this research project under the conditions described.

_____Signature _____Date

I give my permission to be videotaped for this research project, as described in the Informed Consent Form, and for the purposes of education at the University of Florida Health Science Center

_____Signature _____Date

I give my permission to be videotaped for this research project, as described in the Informed Consent Form; for the purposes of education at the University of Florida Health Science Center; and for presentations at scientific meetings outside the University.

_____Signature _____Date

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described in sections 18-22 above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing Date