Deep Brain Stimulation (DBS) for Treatment Resistant Depression: Exploration of Local Field Potentials (LFPs) With the Medtronic Summit RC+S "Brain Radio" System

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STUDY INFORMATION:

Study Title: Deep Brain Stimulation for Treatment Resistant Depression: Exploration of Local Field Potentials (LFPs) with the Medtronic Summit RC+S "Brain Radio" System

Study Site: Icahn School of Medicine at Mount Sinai, Mount Sinai West

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SUMMARY OF THIS RESEARCH STUDY:

This document explains a research study you might be interested in joining. Participation in the study is voluntary. Your decision will not limit your ability to receive care at Mount Sinai. You should only agree to take part if you understand the study and all of your questions about the research study are answered. If you join the study, the research team must share any new information with you that may change your mind about taking part

The purpose of this research study is to use an experimental device, the Summit RC+S (Medtronic, Inc), to measure changes in the electrical patterns in your brain while you are receiving deep brain stimulation (DBS) for your treatment resistant Major Depressive Disorder (MDD). The information obtained in this study will be used to better understand how DBS affects the brain in people with depression, and how brain activity changes as your symptoms change over time.

If you choose to participate, you will be asked to:

- Have weekly evaluations by the study team (first 8 months of study)
- Reside in the New York Metropolitan area for first the two years of the study

- Share your medical records with us to confirm your eligibility
- Have a treating psychiatrist throughout the study and allow them to share information with the study team and vice versa
- No medication changes for at least the first 8 months of the study
- Collect data from your device and about your mood twice a day, every day for 1 year
- Know how to use and maintain your device and accessories, including battery recharging
- Complete interviews and assessments about your medical/psychiatric history and mood, which will be videotaped
- Have neuroimaging procedures
- Have EEGs
- Provide blood and urine samples
- You or your third-party payer will be responsible for ALL surgical costs related to the study. You will not be charged for the Summit RC+S DBS electrodes or implantable pulse generator (IPG).
- You will not be financially compensated for participating in this study. You may request reimbursement for a portion of your travel expenses to research-related appointments.

Known complications of the surgery and/or the anesthesia used during the procedure can be minor (such as discomfort/pain at the surgical sites) or major (including brain hemorrhage, stroke, or, rarely, even death). Secondary complications include device failure, which can result in clinical worsening or additional procedures to replace device components. A complete list of all reasonably foreseeable risks associated with participating in this study is included later in this form.

You may not benefit from taking part in this research if your depression symptoms improve. Deep Brain Simulation is not an FDA approved treatment for depression, and the device has not been approved by FDA for use in or the treatment of any disorder.

Instead of participating in this research, you may pursue other forms of treatment that you have not tried before and you can discuss treatment alternatives with your psychiatrist.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

This research study will be fully explained to you by a member of the study team. Feel free to ask all the questions you want before you make a decision about whether or not to participate. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

You may qualify to take part in this research study because you are between the ages of 25 and 70, have depression symptoms that have been resistant to treatment, and you have expressed interested in receiving deep brain stimulation (DBS). You may qualify to receive DBS if your depression has not improved with multiple treatments, including 4 different antidepressant medications, psychotherapy, and/or electroconvulsive therapy (ECT).

You cannot participate in this study if you have: bipolar disorder or other serious mental illnesses other than major depressive disorder (such as schizophrenia, posttraumatic stress disorder, panic attacks, borderline personality disorder), current drug/alcohol abuse, a neurological disorder (like Parkinson's, Alzheimer's disease, past stroke), have an unstable or life-threatening medical illness, or have a implanted electrical device (such as a pacemaker). You cannot participate if it is not safe for you to have a MRI. Also, you will not be able to participate if you have a medical condition that requires, or will likely require in the future, repeated MRI scans or diathermy. It is unknown if the Summit RC+S device and all of its components are MRI-compatible, so you WILL NOT be able to receive an MRI after being implanted with this device. You cannot participate if you are pregnant or planning to become pregnant during the study.

You must be under the care of a psychiatrist to be in this study, and you must be willing to allow the study team and your psychiatrist to share information. You must be healthy enough to have general anesthesia and brain surgery. You must be willing and able comply with all study procedures and proper use of the DBS device. Also, you must live in the New York City metro region within reasonable commuting to the study location to participate, as well as have a designated caregiver

available to help you oversee your depression symptoms, post-operative care, and to comply with proper device operation procedures, as necessary. These procedures are described in detail below.

Your participation in this research study is expected to last about 10 years: about 12 months in the acute phase of the study starting at the time of surgery, 1 year of monitored follow-up, and then 7 years of ongoing, long term follow up.

There are 10 people are expected to take part in this research study at the Icahn School of Medicine at Mount Sinai, Mount Sinai West.
Funds for conducting this research are provided by the National Institutes of Health, the Hope For Depression Research Foundation, and the Wellcome Leap Fund. In addition, the company who manufactures the DBS device used in this study, Medtronic, has agreed to provide the Summit RC+S research device free of charge, but they will not contribute to or financially support this study in any other way.

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.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study, you will be responsible for the following things:

- Attending all study-related appointments, as scheduled
- Operating the Summit RC+S DBS device and all accessories, as indicated
- Collecting data about your device function, mood, and LFP recordings daily for 1 year
- Being vigilant as to the status of your battery and recharge, as needed
- Maintaining a designated caregiver throughout the study to help with device operation, monitor your condition, help to get you to appointments, etc.
- Taking your medications as prescribed (including using appropriate methods of birth control for individuals of childbearing capacity, as per the “Description of What’s Involved” section)
- Maintaining your current treatment and keeping appointments with your existing psychiatrist

- Informing the research team about any side effects, mood changes, or device issues in a timely fashion as they arise

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DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved. This study will be carried out in several stages over 10 years, which is the battery life of the device. These will include:

- Screening and Pre-surgical evaluation
- Baseline Assessments
- DBS implantation surgery
- Acute stimulation testing and in-person recordings
- A 52 week (approximately 12 month) active stimulation phase with daily LFP recordings at home
- A 1-week discontinuation with daily LFP recordings (after 6 months of ongoing DBS)
- A 1-year continuation phase with resumption of DBS and intermittent LFP recordings
- An approximate 7-year naturalistic follow-up phase with ongoing DBS

These stages are described in detail below. The procedures that take place in this study will be conducted at the Center for Advanced Circuit Therapeutics (C-ACT), a research unit at the Icahn School of Medicine located at Mount Sinai West, part of the Mount Sinai Health System.

Screening and Pre-surgical Evaluation (at least 4 weeks prior to surgery)

After you have signed this consent form indicating that you want to participate in the study, you will be screened to see if you are eligible to participate and complete the study procedures. To ensure that you qualify for this study, you will have a comprehensive evaluation. You will be asked, both in interviews and with questionnaires, about your current and past physical and mental health, as well as information about your use of drugs and alcohol. Individuals who are currently using substances that can increase the risk of DBS or who are pregnant or breast feeding will not be able to participate in this study. This screening should take about one to two hours. It is possible that, after completing the screening, you might not be eligible to participate. If so, you will not complete any further testing or assessments.

Release of Information

You must allow us to review your medical records to confirm your eligibility to participate, including psychiatric and pharmacy records and records regarding prior hospitalizations. This is to document the previous treatments you have received for your symptoms, when you received them, and the effect they had on your symptoms, if any.

Psychiatric Examination

The clinical rater and study psychiatrist will interview you about your medical and psychiatric history. This will include a detailed psychiatric interview and rating of your depressive symptoms. A second psychiatric evaluation will be done to confirm diagnosis of Major Depressive Disorder. This will last about 3 hours in total and may be conducted over several days.

Neurosurgical Examination

You also will meet with the study neurosurgeon, Dr. Brian Kopell, and his staff, who will explain the planned surgery to you. As part of the preoperative assessment, your medical history will be reviewed, and a detailed physical examination will be performed. Also, a small amount of blood (about 3-4 tablespoons) will be drawn and used to test for medical illnesses, and a urine sample will be collected to test for medical illnesses, pregnancy, and evidence of drug use. An electrocardiogram (EKG) will also be performed, which records the electrical activity and rhythm of your heart from electrodes placed on your chest. The neurosurgeon will review your examination and test results to make sure that you are medically healthy enough to undergo brain surgery to implant the DBS device. This appointment will last approximately one hour.

Baseline Assessments (4 weeks prior to surgery)

After you have been deemed eligible to participate and have decided to receive DBS in the study, you will come to the Center every week to complete the following study-related procedures:

Weekly Mood Ratings

Every week during the 4-week pre-surgery period, you will meet with the clinical rater and study psychiatrist, who will rate your depression symptoms and monitor your condition. Your mood will be measured with a number of questionnaires. These study visits will last approximately 2 to 3 hours

each. You will also be asked to complete online questionnaires at home, which will take about 30 minutes per day.

Pre-Surgical Magnetic Resonance Imaging (MRI) scan

Also, prior to surgery, you will undergo a magnetic resonance imaging (MRI) scan, which will be done under general anesthesia. The MRI helps to plan where the electrodes will be placed during your surgery and should take about 2 hours. This procedure is described in more detail below (page 11).

Pre-Surgical Positron Emission Tomography (PET) scan

In addition to the pre-surgical MRI, you will also have an additional neuroimaging procedure called positron emission tomography, more commonly called a PET scan. The PET scans in this study will be done to see how DBS changes how your brain functions over time. This scan will be done before you receive DBS, and it will be used as a baseline to compare to later scans. This scan session will take about 1 to 2 hours (only about 30 minutes in the scanner itself); this procedure is described in more detail below (page 12).

Medications

You may continue to take antidepressant and other medications during this study. You must stay on the same antidepressant(s) at the same doses for 4 weeks before surgery and at least the first 8 months following surgery (unless your depression worsens severely or you develop side effects). The study team will work with you and your psychiatrist to lower the dose or stop your use of certain medications before the DBS surgery, including stimulants, antipsychotic, and benzodiazepine medications.

Summit RC+S System

Components of the DBS system include:

- An **electrode**, which consists of insulated wires with four electrical contacts to deliver stimulation
- An **Implantable Pulse Generator (IPG)**, which is the power source and LFP sensor for the device
- An **extension cable**, which connects the electrode to the IPG (power source)

The IPG is a metal “can” about 2 inches in diameter and about ½ inch thick that is inserted like a pacemaker under the skin of your chest. It contains a small battery that produces the electrical impulses

needed for stimulation, as well as the sensor that measures the LFPs. There is also a cable placed under the skin in your neck that connects the IPG in your chest and the electrodes under your scalp.

DBS Implantation Surgery

Once you have completed all baseline testing procedures, you will have the Summit RC+S system implanted by the study neurosurgeon, along with the researchers.

You will be admitted to Mount Sinai West Hospital on the morning of surgery. First, under local anesthesia, a frame required for the operation will be secured to your head to ensure accurate, stable positioning of your head throughout the procedure. Once the frame is placed, you will be moved to the operating room table and put to sleep. Once asleep, an X-ray Computed Tomography (CT) scan will be performed (described in detail later in this form). Then, two small incisions (about 2 inches each) will be made through your scalp, and two holes will be drilled in your skull (one on each side of your head). The neurosurgeon will then insert the two small electrodes into the predefined locations.

Once both electrode leads are in place, the location will be confirmed by another CT scan.

Then, the extension cables that connect the electrodes to the battery will be tunneled under the skin behind your ear and connected to the IPG. The IPG will be placed in your chest wall below your collarbone, just under the skin. This portion of the procedure will take approximately 1 hour.

Following surgery, you will have another CT scan to check your brain for any unexpected events that may have occurred during surgery. You will receive routine postoperative care, including pain medication and wound care. You will meet with the neurosurgical staff and study psychiatrists each day you are in the hospital.

Acute Stimulation Testing Session & Initiation of Active Stimulation (1 to 2 days after surgery)

Acute Stimulation Testing Session

Before you are discharged from the hospital after your surgery, the study team will test different kinds of stimulation with your RC+S device. This testing will last about 4 hours in total. This testing will be repeated monthly during the first 6 months of the study (active stimulation phase), which will be combined with scalp electroencephalography (EEG; described in detail later in this form).

24 Week Active Stimulation Phase

After the acute testing session is complete, the DBS stimulator will be turned ON, and you will begin to receive continuous active brain stimulation. During this time, you will 1) continue to do the online questionnaires and record your brain activity twice a day and 2) come to C-ACT for weekly visits with the research team.

Summit RC+S System Accessories

You will be provided with equipment for use in the study, which will allow you to 1) recharge your IPG battery and 2) to record your mood and brain signals. These are briefly described on the study information sheet. You will need to keep the various components charged and in working order at all times. The study team will show you these items during your preoperative visits, and you will be taught how to use them before you leave the hospital.

Daily Device Monitoring and Data Collection Procedures: Active Stimulation Phase

Twice each day (ideally once between 7am-9am and once between 5pm-7pm), you will use the tablet (referred to as the Patient Therapy Module or PTM) to: check your device functionality, answer questions about your mood, and have your DBS device record brain activity data. LFP data will be collected with the stimulator ON and OFF for 5 minutes each. Each session will take about 20 minutes (40 minutes total per day). This type of short interruption in stimulation (5 minutes twice per day) has not been shown to have a negative impact on depression symptoms in the past, and you are not expected to experience any adverse effects associated with data collection procedures. Failure to properly maintain and recharge the stimulator will result in loss of DBS stimulation, which may have a negative impact on your clinical condition. If you encounter any problems during data collection, you or your caregiver should contact the research staff, and someone will assist you, as appropriate.

Event Recording

The device being used in this study provides the opportunity to gather information about what your brain is doing when you experience emotional events in daily life and any transient changes in your mood. If something happens during your day that you feel is important for us to know about, you can use your tablet to capture data about this event. This process is similar to the daily data collection procedures and are described in the information sheet.

Weekly Study Visits: Active Stimulation Phase

During the first 6 months of stimulation, you will return to the DBS laboratory once per week to meet with the research team. You will complete the mood ratings and assessments, which are the same as the other weekly study visits. These sessions will last approximately 2 to 3 hours each.

Postoperative PET and CT scans

Two weeks after you leave the hospital, you will have another PET scan to see what changes, if any, have occurred in your brain activity after device implantation and DBS stimulation exposure. This will also be done again two weeks later (4 weeks after surgery) and 6 months after surgery. These scans will be the same as the PET scan you received before surgery and is described in detail later in this document (page 12).

Also, four weeks after you leave the hospital, you will have another CT scan. The scan will be the same as the other CT scan you received before the implantation surgery, which is described in detail later in this document (page 11).

Stimulation-Off Testing (6 months after DBS ON)

At the end of the 6-month active stimulation phase, your DBS stimulator will be temporarily turned OFF for 1 week during a two-week period. The LFP sensor will still be ON, and you will continue to collect data from the device and about your mood twice daily. At the end of the OFF week, the device will turn itself back on, and DBS will resume using the previous settings. You will not be told when the device will be turned off. Though worsening of your depression symptoms is not expected with this short discontinuation, you need to inform study personnel as soon as possible of any noticeable changes in your clinical condition.

2-Year Follow-up Phase (beginning 8 months after surgery)

Following the 6-month active stimulation phase and the discontinuation experiment, you will transition to the long-term follow-up phase of the study. Daily assessments and LFP measurements will continue to be recorded from the Summit RC+S device, as done in the first 6 months. Less frequent recordings will be performed, and you will not need to submit recording data if your depression is improved after completing a full year of ongoing DBS. Computerized Adaptive Test of Mental Health, or CAT-MH, will ask you questions about your mood, anxiety, suicidal feelings, and life quality.

You will continue to meet with the study team and psychiatrists, and adjustments to the stimulator settings and your medications will be made based on how you are feeling. The frequency of office visits during this phase will depend on your condition; however, you will be seen at least: once a month for the first 6 months of this phase (up to 1 year after surgery), every 3 months for the next year (year 2), and every 6 months thereafter until the end of the study. At each visit, you will meet with the study psychiatrist, and the clinical rater will complete the mood ratings and assessments you previously completed weekly. These study visits will last approximately 2 to 3 hours each.
Based on average stimulation parameters and the planned recordings, it is anticipated that the original RC+S IPG will remain active for approximately 9 to 10 years.

Battery Replacement and Long-Term Naturalistic Follow up

When the battery in your device no longer charges efficiently, you will be scheduled for surgery to have it replaced. The Summit RC+S IPG implanted in your chest will be removed and replaced with a commercial device (Medtronic Percept RC). This device provides identical stimulation to the brain as the Summit RC+S, and similarly allows recording your brain activity and recharging of the system as before but with a different hand held device. At the time of IPG replacement you will be instructed in their use. The frequency of study visits during this phase will continue to depend on your condition and depression symptoms. If you are not local to the New York City area, a Medtronic representative will be found closer to your area to download your device data. The costs of the battery replacement surgery will be the responsibility of you or your third-party payer (i.e. your health insurance carrier). The risks of this replacement are the same as those of the initial implantation of the IPG in your chest. The brain electrodes and connection cables will not be modified.

Additional Procedures

The procedures described below will be performed one or more times during the study. These include:

<u>Magnetic Resonance Imaging (MRI) Scan</u>

MRI uses strong magnetic fields and radio waves to obtain detailed images of your brain's structure and function. The MRI will take about 2 hours. Having ANY METAL in your body that has not been deemed safe for use in the MRI will exclude you from having the MRI, and, as a result, you will not be permitted to participate in the study. Also, once you are implanted with the RC+S device, you will not

be able to have an MRI, as it is not known if all the components of the device are MRI-compatible (described in "Risks of MRI" section, page 20).

Once your RC+S battery is replaced with. Percept-RC battery, it will be possible to have MRI scans.. However, there are safety precautions that must be followed and the Medtronic representative will explain those to you at the time of IPG replacement. You will always need to disclose your DBS system to your medical doctors or any radiology department should you require an MRI scan.

In this protocol, the preoperative MRI will be conducted under general anesthesia, as is the standard practice of the implanting neurosurgeon (Dr. Brian Kopell) for all his DBS cases performed at Mount Sinai West. The risks associated with general anesthesia are discussed later in this document ("Risks of Surgery, Anesthesia, and DBS Treatment," page 17).

High-Resolution Computed Tomography (CT) scan

Three CT scans will be performed in this study (one just before, during, and 1 month after surgery) to plan/perform the procedure and verify the final location of the DBS electrodes to select the optimal contacts to be used for your chronic stimulation. Each scan will last about 15 minutes. Known risks associated with these scans can be found in the "Risks of CT Scans" section of this document (page 20).

Positron Emission Tomography (PET) scan

A positron emission tomography (PET) scan is an imaging test that shows how different regions in your brain and body are functioning. A PET scan uses a radioactive drug (tracer), called 18F-fluorodeoxy-glucose (FDG), to measure brain metabolism, which is an index of brain activity. PET scans will be performed 4 times during the study: one scan before surgery, one scan 2 weeks after surgery, one scan 4 weeks after surgery, and one scan 6 months after surgery. You will be given detailed instructions on how to prepare for your scan. Known risks associated with PET scans are described below (page 20).

Total session time will be 1 to 2 hours each, with about 30 minutes inside the scanner. Once you arrive for the scan, an intravenous line will be placed in your arm, and you will receive the injection of the radiotracer. If you can get pregnant, a pregnancy test will be done immediately prior to receiving the

tracer injection to ensure you are not pregnant, as radiation exposure can be detrimental to a developing fetus. You will lie quietly awake with your eyes closed for 30 minutes while the tracer travels to your brain. After this delay, you will lie down in the scanner, and images of your brain will be obtained. You will need to lie still and remain awake throughout the scan.

Videotaping

To provide an audiovisual record of your appearance and behavior during this study, the study team will videotape a portion of every study visit in every phase of the study. The study team would like to see if there are changes in your facial expressions, vocal inflection, or word choice. The research team will analyze these video and audio recordings to determine if there are identifiable changes in your appearance and behavior due to DBS and compare them to your clinical ratings and LFP data, which may identify a potential biomarker of early depression recovery that can help guide treatment decisions in the future. These videotapes will be maintained as part of your study record. Information about how this data will be stored and provisions to protect your privacy are listed below in the "Privacy Risks" and "Maintaining Confidentiality" sections of this document (pages 22 and 27, respectively).

Electroencephalography (EEG)

You will undergo several EEG sessions in the C-ACT lab over the course of the study, which will be analyzed in combination with the recordings from your DBS device. EEG recordings will be scheduled once before surgery and monthly thereafter for the first 6 months. By placing a cap on your head that has electrodes placed in it, EEG can show us what your brain is doing while you have the cap on, and your brainwave activity will be recorded.

Pre-operative EEG. After the cap is applied, your brain's electrical activity will be continuously recorded while you complete some tasks, which will take about 3 hours.

Post-operative EEG. The study team will use EEG to record your brain's electrical activity while you undergo the same procedures that are used in the acute electrode stimulation testing session described earlier (page 8). Also, an additional procedure will be done in this session during which a precise, short burst of stimulation will be applied to one side of your brain at a time and record resulting EEG data to see how the electric current affects the signals from your brain. During this session, the effects of stimulation on your mood and behavior will be recorded. These procedures will last about 3 hours each

time. The session that will occur after the sixth month of active stimulation will be longer and can take place over 2 days, if necessary. The EEG data collected in this study will provide new information as to how DBS improves symptoms of depression. The type of EEG being done in this study is different from the kind that a doctor might order to evaluate a potential medical problem.

Meetings with the Clinical Psychologist

During your time in the study, you will meet every other week with the Center's licensed clinical psychologist, both before and after DBS surgery. This is a PhD-level mental health professional who will develop a cognitive behavioral therapeutic plan for you during the course of your DBS treatment.

Activity Monitoring

You will be asked to wear a wrist-worn activity tracking monitor periodically during the study. Like the video/audio analyses, this data will be used to to see if changes in movement may also correlate with or be predictive of clinical improvement in depression symptoms and/or response to DBS. To protect your privacy, the device used is not capable of tracking your location.

Blood Samples

As part of your neurosurgical evaluation, you will have a blood sample drawn (about 3-4 tablespoons) to do tests to make sure you are healthy enough to have surgery and do not have any existing problems that may make the surgery and/or anesthesia used more dangerous for you.

If you can possibly get pregnant, a urine test for pregnancy will be done before you begin the study and the pregnancy test will be repeated every throughout the study.

You cannot be included in the study if you are or become pregnant, as this study has DBS treatment with potential risks to a developing fetus could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study DBS treatment could harm your baby. The risks to an unborn fetus from DBS treatment in general or from the specific device used in this study is not known at this time.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

All birth control methods (other than abstinence and sterilization) are only effective if you use them properly, start them at least one month before you begin the research study, and continue using them throughout the research study and for one month after the research study ends. If you are unsure whether the method of birth control you use is approved to use while you are in this study, you should ask the Lead Researcher before you begin the study. If you are less than one-year post-menopausal, you could still become pregnant. If you or your partner becomes pregnant, or may be pregnant, at any time during the study, you must tell a person from the research team immediately. The team may stop the study drug and refer you/your partner to an obstetrician/gynecologist for follow-up.

Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Privacy Considerations

Because this project involves the use of medications or a medical device, a note must be included in your electronic medical record that you are taking part in the research. This way, anyone involved in your medical care will know that you are a study participant, and they can work to avoid any problems or negative outcomes that could arise if they do not know.

Limitations of the Summit RC+S system

You should know that the device being used in this study is different than other DBS systems, and, as such, changes to the stimulation parameters can only be made by personnel at Mount Sinai. As of right now, no other facilities use the RC+S device in depression research. If other doctors provide routine clinical services to DBS patients with commercially available Medtronic devices, they will not be able to help you or program your device. You will need to come to Mount Sinai to have any changes made. If you are no longer willing or able to reside in the New York area during the first 2 years of study participation or receive your DBS programming at Mount Sinai at any point, you will be withdrawn

from the study. A description of the procedures related to study exit, as well as options for retaining/removing your DBS device, can be found in the "Ending Participation in the Research Study" portion of this document. Study participants whose personal circumstances require them to move away from the New York metro area after the first two years of the study may be permitted to continue study participation with the RC+S device on a case-by-case basis after careful review by and consensus of the study investigators. You should consider this when you are deciding whether or not you want to participate in this study.

Contraindications to DBS (Prohibited Procedures)

You will not be able to receive the following procedures once you are implanted with the Summit RC+S system. Further details can be found in the study information sheet.

Diathermy (deep heat treatment).

Study participants with DBS cannot receive shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy anywhere on your body. Energy from diathermy can be transferred through the DBS system, which can cause tissue damage and result in severe injury or death.

Magnetic Resonance Imaging (MRI).

Once implanted with the RC+S device, you will not be able to have a MRI. Performing MRI with this device implanted in your body can result in serious and permanent injury, including coma, paralysis, or death. If you need regular MRIs to monitor another medical condition, you cannot participate in this study. If a MRI is needed to evaluate a clinical problem, you must first contact one of the research physicians, who will coordinate with the necessary parties to decide on a course of action.

Once your RC+S battery is replaced with a Percept-RC battery, it will be possible to undergo MRI scans. However, there are safety precautions that must be followed and the Medtronic representative will explain those to you at the time of your IPG replacement. You will always need to disclose your DBS system to your medical doctors or any radiology department should you require MRI scans.

Electroconvulsive therapy (ECT)

The safety of ECT in study participants who have an implanted DBS system has not been established. If your depression worsens and you choose to have ECT, the study team will discuss with you the

potential risks of applying ECT to subjects with DBS devices or whether the DBS device should be removed beforehand.

Transcranial magnetic stimulation (TMS) therapy
The safety of TMS in study participants who have an implanted DBS system has not been established at present. In addition, there is no established clinical indication for receiving TMS and DBS simultaneously. No additional or adjunctive antidepressant treatments of any kind should be initiated without receiving the explicit approval of the Lead Researcher or site clinical personnel.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

There may be costs to you for taking part in this study. You or your third-party payer (i.e. your health insurance carrier) will be responsible for ALL clinical costs related to the study, including but not limited to preoperative testing (labs, EKG, MRI), implantation surgery, postoperative surgical care, and postoperative CT scan. The team will work with you and your insurance company prior to receiving the surgery to address coverage of your clinical expenses. The study team will provide you a list of procedures and fee schedule for out of pocket costs before surgery so you will know what to expect. The device manufacturer, Medtronic, Inc., will provide the DBS electrodes and Summit RC+S research device at no cost to you as part of the study. However, you or your third-party payer will be also be responsible for the cost of the replacement device and the surgical costs of its implantation at the point of battery depletion.

You will not receive compensation for being in this study, but you may request reimbursement for your travel to the study site for research-related appointments. The maximum amount to be reimbursed is $15 per visit, and a maximum of 50 visits will be reimbursed over the course of the study. Receipts must be submitted in order to receive reimbursement, which will be provided in the form of checks issued no more than once per month. Checks require some time to be processed.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally, this happens if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

POSSIBLE BENEFITS:

Deep Brain Stimulation is NOT FDA approved for the treatment of Major Depressive Disorder. This study is not designed to benefit you personally. [There is a possibility that your depression symptoms may improve with the SCC DBS received in this study. However, this is a possibility and not a certainty. The Summit RC+S device being used in this research has not been approved for use in any condition, but it delivers current to the brain in a similar manner to conventional, commercially available DBS devices indicated for other conditions. The information obtained from this study will aid in understanding treatment resistant depression, how it effects the brain, and the effects of SCC DBS in this context.

POSSIBLE RISKS AND DISCOMFORTS:

Risks of Surgery, Anesthesia, and DBS Treatment

As with surgery for any medical problem, there are risks involved both from having the surgery and/or the anesthesia used during the procedure. The neurosurgeon, Dr. Kopell, and his staff will discuss any and all risks with you in detail and answer any questions you may have when you meet with them, as well as procedures to mitigate these risks, treatments available for given complications, and consequences of these effects should they occur. A summary of the known side effects and complications associated with DBS device implantation are listed below. The estimated rates of the effects listed have largely been based on those experienced by study participants receiving DBS for Parkinson's disease, which is the largest patient group receiving DBS at present. In addition, the specific experiences of patients receiving DBS for depression in research studies has also been provided in the study information sheet.

The complications of DBS surgery are well established and relate to 1) surgical complications at the time of implantation (such as hemorrhage, seizures, stroke) and 2) secondary complications due to failure of the device, infection, or stimulation of parts of the brain adjacent to the ones intended. The risk of death associated with the general anesthesia used for the preoperative MRI and implantation of the IPG is small (less than 1 in 20,000 people). More common risks of surgery are pain, discomfort, and/or swelling at the sites of the incisions in the head and chest, as well as at the sites where the pins of the stereotactic frame are placed. If these problems occur, they generally go away within one week

for most people. These risks are the same for anyone receiving DBS surgery and are not specific to those receiving it for depression.

Risk of Infection, Device Malfunction, Adverse Reaction to Device Components

It is possible that the device and/or its components may become infected. This could cause an infection not only in the area of the implanted device but also an infection that involves the whole body. Such an infection would require treatment with antibiotics and, possibly, surgery to remove the DBS system. The risk of infection or malfunction of the DBS device and/or IPG is about 10.6%. It is also possible that an implanted electrode may move, break, or become dislodged requiring another operation to correct. There is also a chance of having an allergic reaction to the device or any of its components requiring device explantation, as well as a risk that a component of the device may cause damage to your brain or other parts of your nervous system or cause tumors (benign or cancerous) due to materials that compose the leads.

Risk of Clinical Worsening / Onset of New Psychiatric Symptoms

As DBS is an experimental procedure in major depressive disorder, it is possible that the symptoms of your depression will not improve, or even become worse, with DBS. If your depression does not improve over time or you experience worsening of your psychiatric condition, the investigators will discuss with you the option of changing the dose of stimulation, the location being stimulated, making adjustments to your medications, discontinuing active stimulation, and/or removing the device. You should promptly inform study personnel as to any changes in your symptoms.

Need for Additional Surgical Procedures

It may become necessary to remove the DBS device. Reasons for removing the device include damage to the device or infection that does not adequately respond to antibiotics. Removal of the device has a very low risk of serious complications (less than 1 in 1,000), but they are the same as those associated with surgical implantation of the device stated above (see page 17).

Risks Associated with Battery Replacement(s)

The estimated IPG battery life of the RC+S device using standard stimulation parameters is approximately 10 years from the time of implantation. Battery life may be shorter in this study due to the recordings from the RC+S sensor, which uses extra battery power, but the additional power the

device consumes may be offset by the ability of the battery to be recharged. At the end of battery life, another minor surgical procedure will be required to replace the IPG. The IPG used for replacement will provide identical stimulation to the brain but cannot monitor brain activity. The risks of this procedure are similar to the risks of having the first IPG implanted in your chest, namely discomfort or pain at the site of the incision, infection, or risk associated with anesthesia (see page 17). The need for repeated surgeries to replace the battery is one additional risk of participating in this study.

Risks of Battery Depletion or Interruption of Stimulation.

If your DBS system is not working properly, it is possible that your depression symptoms can return. One reason that the device may not work properly is if the battery is not adequately charged. For this reason, it is EXTREMELY IMPORTANT that you that you monitor the status of your battery on a daily basis. In study participants who received DBS for depression with other devices, temporary discontinuation of stimulation (lasting hours to days) has not been associated with any noticeable behavioral changes. Controlled experiments of DBS discontinuation observe a slow decline that develops over several weeks characterized by decreased motivation, interest, and activities, followed by a late change in negative mood. Abrupt changes in sadness, anxiety, or sudden thoughts of suicide have not been observed to date. You should report changes in your symptoms or device problems to the study personnel as soon as possible.

Risk of Other Device Malfunction

Loss of Sensing Capability

Should the RC+S device experience a failure in sensing capacity only, the research team will first attempt to reestablish this functionality using the programming software. If the sensing function of the RC+S cannot be recovered and the device is otherwise operational (e.g. the ability to deliver stimulation has not been compromised), no further action will be taken, as sensing is being using for research purposes only and has no bearing on clinical outcome. If this were to happen, you would no longer be able to collect LFP data in the protocol, but you would still receive DBS stimulation and continue to complete all other study procedures, as scheduled.

Risks of Other Study Procedures

Risks of MRI

Pre-surgical scans. There are no known risks of exposure to magnetic fields of this strength in healthy people. While there have been no reports of any harmful long-term effects caused by MRI magnets of the same or even higher strength as those used in this study, the long-term effects of being placed in a magnet of this strength are unknown. MRI is generally painless, but it can be uncomfortable or difficult for you to lie still in the scanner. Rarely, you might also experience stimulation of the nerves in your body, which feels like a gentle tap or tingling sensation. If this happens, the sensations generally stop when the scan is stopped. You also may be bothered by feelings of anxiety or even claustrophobia, since the MRI is a confined space.

The risks associated with the general anesthesia used in this procedure are well known and have been discussed previously in this document ("Risks of Surgery, Anesthesia, and DBS Treatment", page 17). There are no additional risks of anesthesia use in this context, and all equipment used is compatible with the MRI. The procedure will be supervised by an anesthesiologist in its entirety to ensure your safety. During the evaluation process, you will be thoroughly screened for factors which may make having general anesthesia dangerous for you. As it is also required for implantation of the DBS system IPG, individuals who cannot receive general anesthesia will be excluded from study.

Risks of PET and CT Scans

You will have several PET and CT scans as part of the study and the DBS implantation process, so your participation in this research study includes exposure to radiation from x-rays or gamma rays. Since DBS is not an approved treatment for depression, this radiation exposure is for research purposes only and is in addition to any radiation needed for your medical care. However, the amount of radiation you will receive from the CT scans is the same as that of similar patients who receive DBS outside of a research study (i.e. if a patient receives DBS for Parkinson's disease at Mount Sinai, this is the same type of scan they would receive). The radiation to which you are exposed from the PET scans is in addition to the amount received by others who receive DBS for clinically approved indications but is necessary to obtain the desired research information. X-rays and gamma rays from natural or medical sources can damage the genetic material (DNA) in your cells. At low radiation exposures, the body is usually able to repair the damage. Radiation risk is believed to be related to the total lifetime exposure. You should think about your own history of radiation exposure from tests

(like x-rays or CT scans) in deciding about the radiation in this study. If you have questions about the total amount of radiation you will be receiving, you should ask your doctor.

The estimated radiation exposure that you will get for this research study will be 36.04 mSv (an mSv is the scientific unit of measurement for whole body radiation dose, or 'effective dose'). The greatest annual exposure (36.04 mSv) is projected to be in year 1. This exceeds the 6.2 mSv that the average person in the United States gets each year from both natural sources like the sun, outer space, air, food, and soil, as well as from medical procedures. It is less than the 50 mSv of radiation that is allowed each year for people who are exposed to radiation in their jobs.

The scans being done in this study will not use any additional contrast agents. As with MRIs, you can experience discomfort by being in the scanner or have trouble laying still during the scan, and you can experience claustrophobia during the scan. Since PET scans will require an injection of the radiotracer, there are risks associated with the IV placement, which are described in the next section.

Risk of Collection of Biological Samples / Intravenous Catheter Placement

For most people, having blood drawn or an IV does not cause any serious problems. However, there is a risk of pain, bruising, and the slight possibility of infection at the place where the needle is inserted. If this happens, the effects usually go away in a few days on their own. You may feel dizzy or may faint. The risk of having blood drawn or an IV placed in this study is no different than what you would encounter with a routine blood test done at a doctor's office or an IV used for other medical purposes.

Risks of Electroencephalography (EEG)

EEG is a safe procedure that uses electrodes to measure brain activity. Because the electrodes only record activity, they will not produce any sensation or cause you discomfort, nor will the EEG interfere with your DBS stimulation. Sometimes, the cap and electrode gel can make you feel itchy, which usually goes away when you take the cap off and remove the excess gel.

Risks of Screening and Assessments

The screening, interviews, and tests can be time consuming and tiring. As part of the psychiatric assessments, you will be asked sensitive questions, but the questions asked are similar to those you are asked during your routine psychiatric and medical care. It is possible you will feel upset, tired, bored,

or anxious during the interviews. If you do, you can decide not to answer specific questions, ask for a break, or stop the interview or test.

Risks of Activity Monitoring

There are no known risks of wearing the activity monitoring watch. You will not be tracked about where you go, just how much you move.

Risks of Physiological Measures

There are no known risks associated with the heart/breathing rate, EKG, skin conductance, or oximetry monitors used during and/or after surgery.

Privacy Risks

Your name and other information that could directly identify you (such as address or social security number) will never be placed into a scientific database. Your research data (such as rating scales, LFP measurements, activity monitoring, video recordings) will be deidentified and stored in physically and/or electronically secure locations in the research offices. You name and other personally identifiable information will not be stored in conjunction with the videotapes of your study sessions. Data will only be shared with co-investigators and collaborators working on this project, who will only view the minimal amount of data necessary to complete the scope of their work on this project. The data shared will not identify you by name nor will any other personally identifiable information be connected to your data. Access to the key that can link your data to you personally will be limited to select members of the research staff. Medtronic, the company that makes the device, will know your name at the time your RC+S system is registered, which is done for regulatory and safety purposes. The company will not have access to any other information about you but will reserve the right to update the study team about any safety developments or updates about the device that impact your care. As with any time you share private and personal information, there is always a risk of loss of this private information, but there are procedures in place to minimize this risk and protect the information you share with us. These procedures are described in the “Maintaining Confidentiality” section of this document (page 27).

Economic risks

Taking part in this research study may lead to added costs to you. You and your third-party payer (i.e. your health insurance company) will be responsible for the costs of ALL clinical procedures related

to the study, including but not limited to the implantation surgery, clinical follow-up appointments, and lab tests. The team will work with you and your insurance company prior to receiving the surgery to address coverage of your clinical expenses. However, it is possible that you may have to pay money out of pocket for medical expenses. The device manufacturer, Medtronic, Inc., will provide the DBS electrodes and Summit RC+S research device at no cost to you as part of the study. However, you or your third-party payer will be responsible for the cost of the replacement battery and the cost of its implantation. In addition, there may be other potential economic risks to you associated with study participation, such as missing work or school for study appointments.

Group Risks

Although your name will not be given to researchers, basic information such as your race, ethnic group, and sex may be shared. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or even promote discrimination.

Depression-related Risks

Those with TRD can experience suicidal ideation. As a result, suicidal behaviors, including attempts and completed suicide (death), are possible risks associated with TRD. It is not yet known if Deep Brain Stimulation changes the risk for suicide in study participants with depression. As done in all psychiatric care (including the care you have received for your depression outside of a research study), you will be asked about any suicidal thoughts and/or behaviors you may have been experiencing, as well as your intent to act upon them, as part of your visits with the study psychiatrist and psychologist, as well as part of your clinical ratings. If you are having any of these thoughts and are at risk for acting on them at any time, please contact the research team immediately who will discuss additional treatment options with you as per your individual safety plan, which will be established prior to surgery.

Unforeseeable Risks

This study may involve risks to you that are currently unknown and unforeseeable**.** In addition to these risks, this research may hurt you in ways that are not known. The unknown risks might be minor or might be major (death). DBS and/or use of this specific DBS stimulator may involve other risks that

are not known at the present time. The long-term effects of DBS are not known. You will be informed of any and all additional risks to you as they are identified.

OTHER OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you. For study participants with TRD who qualify to participate in this study, alternative treatment options are limited, due to your past treatment failures. There is one FDA approved alternative surgical treatment for depression called vagus nerve stimulation (VNS), though receiving VNS will make you ineligible to receive DBS in the future. You should discuss other treatment alternatives with your psychiatrist before choosing to participate in this study, including other clinical trials of DBS for depression. The Study Psychiatrists will also discuss potential alternatives for treatment with you and your treating psychiatrist, if needed.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, you will get medical care. Generally, it will be billed to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, copayments, and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Lead Researcher or the research staff. If you decide you want to withdraw from the study after the DBS device has been turned on, the study staff will meet with you to discuss this decision. If you choose to exit the study but have received clinical benefit from SCC DBS and would like to continue receiving DBS for your depression, you will need to have the RC+S IPG replaced with a commercially available product, which can be

programmed by clinicians who care for patients with other Medtronic devices. The study investigators will discuss this option with you to determine if it is appropriate, including evaluating the improvement in and stability of your depression symptoms and your plan for receiving care outside of the study. If you decide that you want to have your DBS device removed for any reason, the stimulation will first be turned off for a minimum of 12 weeks, and the study personnel will then assess your condition. If at that time you continue to want the device removed, you will be scheduled to see the neurosurgeon and set up a time to have the device removed from your body. Regardless of your choice (replacement or removal), you will require an additional surgical procedure, and you will be financially responsible for the cost of this procedure and any device component(s). You will have the option of withdrawing completely from the study or staying in touch so your condition can be monitored in the future.

If you decide to stop being in the research study, you will return to treatment as usual with your existing psychiatrist. If you stop being in the research study, information already collected may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the study doctor can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not to be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If

your data and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent

The Lead Researcher, the funder or Mount Sinai may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns, or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher, Dr. Helen Mayberg, at phone number 212-824-8278.

Alternate Study Contacts:
Isha Trivedi (Clinical Research Coordinator), 212-523-8242
Dr. Brain Kopell (Neurosurgery), 212-523-8340
Dr. Martijn Figee (Psychiatry), 212-523-8681

For medical or psychiatric emergencies during the study after business hours or on weekends:

- Call 911 and/or go to the nearest emergency room. Let the emergency room staff know you are in a research study so they can contact the Lead Researcher if needed.
- Contact Dr. Kopell, Dr. Figee, and/or your treating psychiatrist, as appropriate (i.e. depending on the problem you are having)
- Inform the research team as soon as possible after the event

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are

encouraged to talk to the Lead Researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

One or more researchers has a financial interest that could be affected by the outcome of this research study. This study uses devices manufactured by Medtronic, Inc. Dr. Mayberg, the Lead Researcher of this study, has no financial relationship with Medtronic outside of the contract that gives the research team and this protocol access to their Summit RC+S device. Dr. Mayberg is a named co-inventor on the novel method for using deep brain stimulation (DBS) in the specific region of the brain used here (the subcallosal cingulate area) as a potential therapy for treatment resistant depression. This method had been licensed to Abbott Laboratories, which is a different company than the one that is providing the devices that you will have implanted. Dr. Mayberg has received and is entitled to receive future royalty payments from Functional Neuroscience related to this method. In addition, Dr. Mayberg receives financial compensation as a consultant to Abbott Laboratories for the development of their studies of DBS devices for the treatment of treatment resistant depression. In addition, Dr. Brian Kopell (Study Neurosurgeon and Co-Investigator in this study) receives financial compensation as a consultant for St. Jude Medical, Inc (a manufacturer of DBS devices, which will not be providing the device that you will have implanted).

All industry relationships, Dr. Mayberg's interest in the procedure, and this research study has been reviewed by Icahn School of Medicine at Mount Sinai and their Human Research Protection Program, who have developed a management plan that they must follow. Dr. Mayberg will oversee the protocol procedures and your overall participation during the study. Dr. Kopell will implant your DBS device and will be responsible for your neurosurgical care. However, individuals who do not have a financial interest in this technique will be primarily responsible for evaluating your suitability to receive DBS for TRD, providing study-related care, and assessing your clinical progress over time.

If you have questions regarding paid relationships that your physician/researcher may have with industry, please to talk with them, or check for industry relationships posted on individual faculty pages on our website at http://icahn.mssm.edu/.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?

PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others? As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, telephone numbers, birthdate, dates of admission/discharge, e-mail address, social security number, medical record number(s), health plan numbers, device identifiers, and photographic images. The researchers will also get information from your medical record at Mount Sinai, from your current private doctor(s), and from other facilities where you received medical services (e.g. doctor's offices, hospitals) or medications (pharmacy records). During the study the researchers will gather information by:

- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- reviewing mental health records
- reviewing alcohol and/or substance abuse records, if applicable
- reviewing psychotherapy notes

Why is your PHI being used?

Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at

scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example:

- The Mount Sinai *Program for the Protection of Human Subjects is responsible for overseeing research on human* participants *and may need to see your information.*
- *If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.*
- ***If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.***

Who, outside Mount Sinai, might receive your protected health information?
As part of the study, the Lead Researcher, study team, and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Lead Researcher.)

- The device manufacturer and/or their representative (who will use the results for submissions to the Food and Drug Administration): Medtronic, Inc.
- The sponsoring government agency and/or their representative who need to confirm the accuracy of the results submitted to the government or the use of government funds: National Institutes of Health
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- Research collaborators at Emory University, who are investigators on the study grant and FDA submission and are responsible for study continuity and care of study participants across sites

- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.

Medtronic, Inc., the manufacturer of the Summit RC+S system, will be provided with limited personally identifiable information collected during this study. The identifiable data that may be provided to Medtronic will only include device-related information, which they must report about to regulatory authorities. They will also receive your weekly depression rating scale scores and the LFP data recorded from the RC+S IPG. However, this data will only identify you by your study number, not your name. Medtronic will keep your data confidential in accordance with all applicable laws and regulations. Medtronic may use your data for any purpose in accordance with applicable laws. Any reports or publications about the study or any other research will not include your name or a description of you. Information received during the study will not be used to market to you; your name will not be placed on any mailing lists or sold to anyone for marketing purposes. You agree to allow Medtronic to use your data in these ways.

Results from study tests and procedures that are performed, analyzed and/or read at or for Mount Sinai Healthcare facilities that can be used for healthcare purposes will be placed in any medical record that you have with Mount Sinai Healthcare facilities. In addition, a copy of the informed consent form and HIPAA authorization form that you sign will be placed in any Mount Sinai Healthcare medical record you may have. Persons who have access to your medical record will be able to have access to all results and documents that are placed there, and the results/documents may be used by Mount Sinai Healthcare facilities to help provide you with medical care. Certain state and federal laws and regulations that may prevent the disclosure of research data do not cover any results and documents that are kept as part of your medical record. However, laws such as HIPAA that concern medical records will govern the confidentiality of the results and other documents in the medical record.

In almost all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier. Some records and information disclosed may be identified with a unique code number. The Lead Researcher will ensure that the key to the code will be kept in a locked file or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. The

Certificate of Confidentiality obtained from the Department of Health and Human Services will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others. It is possible that a sponsor or their representatives, a data coordinating office, or a contract research organization, will come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers.

Additionally, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. They are authorized to remove information with identifiers if necessary to complete their task. By signing this document, you are authorizing this access. The results of this research may be published.. However, your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information?
Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?
During your participation in this study, you will have access to your medical record and any study information that is part of that record. The research team is not required to release research information to you that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?
NO! If you decide not to let the research team *obtain, use or share your* PHI*, you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment, or enrollment in any health plans or affect your eligibility for benefits.*

Can you change your mind?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff.
The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from taking part in the research study.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your PHI.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing *your medical records* or asking questions about your *medical history* or conditions*, it is possible that* they may learn information related to your HIV status. *If that is the case, the following information concerns you. If* researchers are not reviewing your *medical records or* asking *questions about your medical history or conditions, then* you may ignore *the following section*.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIVrelated information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Certificate of Confidentiality

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services. This is intended to ensure that your identity as a participant in this research study will not have to be disclosed as a result from a subpoena, for the purpose of identifying you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings other than to the FDA or OHRP as identified above.

The research staff will not share any of your personal information, study data and/or samples with anyone who is not a member of the research team, including any family members or friends, other than those identified above. However, you should know that if it is learned that you or someone else is threatened with serious harm, such as a child or an elderly person being abused, the research team may notify the appropriate authorities if necessary to protect you or others. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. This means that you and your family must also actively protect your own privacy. If an insurer or employer learns about your research participation, and you agree that they can have your research information, then the researchers may not use the Certificate of Confidentiality to keep this information from them.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

ADULT PARTICIPANT:

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

_____	_____	_____	_____
Signature of Participant	Printed Name of Participant	Date	Time [required if used for FDA documentation purposes]

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

_____	_____	_____	_____
Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:

When a witness is required to observe the consent process, it should be documented below (for example, when subject is illiterate, visually impaired, or this document accompanies a short form consent).

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant, and that consent was freely given by the subject.

_____	_____	_____	_____
Signature of Witness	Printed Name of Witness	Date	Time

Future Contact:
The researchers may wish to use your personal contact information to contact you in the future. Do you give the researchers permission to **contact you** in the future to request the collection of additional information about you, discuss how your private information, study data and/or samples might be used, or discuss possible participation in another research study?

Please initial your choice: Yes_____ No_____

If "Yes", please indicate your preferred method of contact: (initial all that apply)
[ ] Email [ ] Phone [ ] Letter [ ] Text

USE OF YOUR DATA
In addition to being used to complete this research study, your personal information (such as, name, address, date of birth, social security number) and study data may also be used and shared for additional (future) research. Before anything is shared, all of your identifying personal information will be removed, and it will be replaced with a code. Researchers are not planning on giving you the details of any of this future research nor the results. That means that a research project might be done that you would not consent to if provided with the details of that research project. You can still be part of the study if you do not allow us to use or share them. Please select Yes or No to each of the questions below. To decline all future uses/sharing please select 'No' each time You have the right to withdraw, at any time, your consent to future use of the data. If you wish to do so, please let the research staff know immediately or contact the Lead Researcher, Dr. Helen Mayberg (her contact information is listed on the first page of this form).

(1) Will you allow the researchers to store your information to use in future research studies?

Please initial your choice: Yes_____ No_____

If no, please stop here. If yes, please continue to the next question and tell us how your personal information, study data and/or samples may be used in future research studies.

(2) The researchers can keep your information stored in one of two ways:

a) Anonymously (no one will know who the data and/or samples came from). If you choose this option, you can't change your mind. So, if you wanted to have your data and/or samples destroyed in the future, the team could not do it as they would not know which data and/or samples were yours.

b) Linked to your identity (using a code that can show the information came from you personally). In this case you could ask for your data and/or samples to be destroyed in the future if you want that to happen. How would you like your information stored? Please initial **ONE** choice:

How would you like your information stored? Please initial **ONE** choice below:

I would like my information stored anonymously _____

I would like my information stored with a link to my identity through the use of a code _____

(3) Do you give the researchers permission to keep the information indefinitely and use it for future studies that are **directly related** to the purpose of the current study?

Please initial your choice: Yes_____ No_____

(4) Do you give the researchers permission to keep the information indefinitely so they can use it for future studies that are **not related** to the purpose of the current study (for example, a different area of research)?

Please initial your choice: Yes_____ No_____

(5) Do you give permission to have your data and/or samples given to other researchers, including those at Mount Sinai, other medical or scientific institutions and for-profit companies, for use in research within the limits you have chosen above?

Please initial your choice: Yes_____ No_____

(6) Do you give permission to have portions of your data and/or samples deposited in large public databases (repositories) for use in research with the limits you may have chosen above? Please read the paragraphs below which explains repositories, then initial your choice:

To do more powerful research, it is helpful for researchers to share information from the people they study. They do this by putting data and/or samples into a repository. A repository is where something is stored safely for a specified period of time. Data and/or samples from one study may be stored in a repository along with data and/or samples from other studies. Sample repositories are commonly called biobanks, while data repositories are commonly called databases. Researchers can then use the data and/or samples from multiple studies to learn even more about health and disease. If you agree to take part in this study, some of your health information might be placed into one or more scientific databases, but they will not share your direct identifiers (for example, name, address, date of birth). These databases are maintained by either Icahn School of Medicine at Mount Sinai, another institution, the federal government, or private companies. Any researcher who wants to do a study using data and/or samples from the repository must apply for permission. There are different ways of reviewing such requests. Researchers with an approved study may be able to see and use your data, along with that from many other people. Researchers may use your information for other experimental testing. Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are always risks associated with data collection and sharing. They are described in more detail in the Risks section of this document.

Researchers will use a Global Unique Identifier, a computer-generated ID, which cannot be linked back to your identity. This is so any data collected from you is linked to one unique ID, so databases operated by the National Institutes of Health can make sure your data is secure and is not accidentally duplicated if you take part in research at multiple sites.

Please initial your choice: Yes _____ No _____

Whether or not you have allowed us to share your data and/or samples with these repositories, the researchers at Mount Sinai will keep data and/or samples collected about you during this research study to use in future research studies consistent with the wishes you expressed above.