Scalar Closed-Loop STN/GPi DBS Based on Evoked and Spontaneous Potentials (Permanently Implanted Medtronic RC+S Studies)

NCT03815656

Document Date: April 30, 2021

DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
Scalar Closed-Loop STN/GPi DBS Based on Evoked and Spontaneous Potentials (Permanently Implanted Medtronic RC+S Studies)

CONCISE SUMMARY

This investigational study evaluates if placing two deep brain stimulating (DBS) electrodes on each side of the brain can improve the symptoms of Parkinson's disease better than placing just a single electrode on each side of the brain. The DBS electrodes will be placed in standard areas of the brain for treatment of Parkinson's disease.

This study plan will involve implantation of clinical DBS electrodes, using two electrodes on each side of the brain rather than just one, and instead of the standard clinical battery or implantable programmable generator (IPG - Medtronic Activa PC), the rechargeable research IPG (Medtronic Summit RC+S) will be implanted. The study will proceed for at least 4 years but the research IPG may last much longer than that (up to 9 years) so there may be a possibility of extending the study.

During this study, you will receive standard clinical, single-site DBS stimulation most of the time, depending on what works best in your individual case. However, a large part of the study is to return for daylong research visits, typically at least once per month, to be able to test the research types of stimulation. Research types of stimulation may also be tested during home "visits" via videoconference.

There are risks associated with the device implantation procedure and electrical stimulation including bleeding, infection, long-term risks of wiring malfunction, and others that need to be discussed in detail, since the Summit RC+S is a research device.

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

You are being asked to take part in this research study because you are undergoing a surgical procedure involving placement of deep brain stimulating electrodes in your brain for severe Parkinson's disease. Research studies include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed in this consent form.

Please tell the study doctor or study staff if you are taking part in another research study. You do not have to participate in this study. Your decision will not change your current or future relations with Duke University Medical Center or its doctors.

Dr. Dennis Turner will conduct the study and it is funded by a grant from the National Institutes of Health (NIH).

Consent To Participate In A Research Study
Scalar Closed-Loop STN/GPi DBS Based on Evoked and Spontaneous Potentials (Permanently Implanted Medtronic RC+S Studies)

As described above, the primary purpose of this study is to determine if placing two deep brain stimulating (DBS) electrodes on each side of the brain in standard areas of the brain (subthalamic nucleus – STN, and globus pallidum – GPi/GPe) can improve the symptoms of Parkinson's disease better than placing just a single electrode at one of the sites on each side of the brain. Additionally, the study will involve long-term research on how to improve DBS stimulation, including development of adaptive stimulation. Adaptive stimulation uses brain activity to determine how and when to stimulate rather than just fixed settings. This mode is similar to a heart pacemaker, which records heart activity and then performs stimulation only as needed (rather than on all of the time). If either dual electrode stimulation or adaptive stimulation is better than standard clinical, single-site DBS stimulation you can stay on the improved stimulation protocol until the end of the study. This study will involve implantation of a next-generation, research implantable pulse generator (Medtronic Summit RC+S IPG or battery) which allows these different types of stimulation. The clinical Medtronic Activa IPG currently available does not permit the study of two electrodes per side nor adaptive stimulation. This study plan will involve implantation of clinical DBS electrodes, using two electrodes on each side of the brain rather than just one, and instead of the standard clinical IPG (Medtronic Activa), the rechargeable research IPG (Medtronic Summit RC+S) will be implanted. The study will proceed for at least 4 years but the research IPG may last much longer than that, so the study may continue depending on funding and support (up to 9 years). If the research IPG and alternative stimulation paradigms work for you, there may be a possibility of extending the research stimulation past the study end time of 4 years. During the study, you will receive standard clinical, single-site DBS stimulation most of the time, depending on what works best in your individual case. However, a large part of the study is to return for daylong research visits, typically at least once per month, to be able to test the research types of stimulation.

The study doctors involved in this study are Dennis A. Turner, M.A., M.D., Department of Neurosurgery, Duke University Medical Center, Jeffrey Cooney, MD, Department of Neurology, Duke University Medical Center, Kyle Mitchell, MD, Department of Neurology, Duke University Medical Center, Warren M. Grill, Ph.D., Department of Biomedical Engineering, Duke University, and Shivanand (Nandan) Lad, M.D., Ph.D., Department of Neurosurgery, Duke University Medical Center. This study is being sponsored by a grant from the National Institutes of Health and Duke University. Portions of Dr. Turner's, Grill's and Lad's effort and the research team's salaries are being paid by this grant. Dr. Lad has received personal compensation as a consultant for Medtronic in the past for his work on neuromodulation and may receive personal compensation from Medtronic in the future. Medtronic developed the research technology (the next generation Summit RC+S IPG) that is being used in the study as well as the standard clinical DBS brain electrodes. However, Medtronic is not the sponsor of this study, which is independently funded by National Institutes of Health through Duke University. Dr. Grill developed a recording technology that may also be used during the DBS implant surgery. Dr. Grill's recording technology has been licensed to Deep Brain Innovations (DBI), LLC, a company that was founded by Dr. Grill and for which he serves as Chief Scientific Officer. Dr. Grill owns a portion of DBI and may receive royalty payments from DBI related to his technology, though not for this specific research use.

DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
Scalar Closed-Loop STN/GPi DBS Based on Evoked and Spontaneous Potentials (Permanently Implanted Medtronic RC+S Studies)

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Dr. Dennis Turner (primary investigator on the study), Dr. Jeffrey Cooney, Dr. Kyle Mitchell, and/or Dr. Shivanand (Nandan) Lad will be your doctors for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?

The overall goal of this research is to understand better how deep brain stimulation treats the symptoms of Parkinson's disease. Besides receiving standard clinical, single-site DBS stimulation (i.e., to either STN or GPi) there is a possibility that stimulating two electrodes together on each side of the brain may improve the stimulation benefit you receive. Additionally, it is possible the adaptive stimulation may show fewer side effects than standard clinical, single-site stimulation, allow a longer time between recharging intervals, or demonstrate improved clinical results. The information we learn in this study may also be helpful for developing automatic adjustment of the DBS device in the next generation of devices.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

This study will be performed on up to 6 subjects with deep brain stimulation for the treatment of Parkinson's disease.

WHAT IS INVOLVED IN THE STUDY?

If you agree to take part in this study, you will be asked to sign and date this consent form. As part of the pre-operative workup for DBS you will undergo neuropsychological baseline studies, testing of your Parkinson's disease on and off medications with the Unified Parkinson's Disease Rating Scale (UPDRS) (on/off test), assessment of outcome measures, including the Parkinson's quality of life scale [Parkinson's Disease Questionnaire (PDQ-39)], and a 3 day patient diary of symptoms, called the Hauser diary. All of the UPDRS assessments you complete as part of this study will be video recorded. These recordings will be sent to a "blinded" reviewer for rating. This means the reviewer will not know if you are on or off medications and/or DBS stimulation for each video. This allows us to have an unbiased comparison of how the different types of DBS stimulation we are studying affect your motor symptoms. Some of the other assessments you do at the daylong research visits may also be video recorded so we can compare how your symptoms respond to different stimulation settings. All of these electronic video recordings will be stored in a secure computer drive that can only be accessed by members of the study team.

This study involves two features different from the standard clinical DBS procedures. First, dual electrodes will be placed in standard treatment areas on each side of the brain (i.e., STN and GPi rather than just STN or GPi) to see if dual electrode stimulation is better than a single electrode, and to compare the two different sites of stimulation in the same subject. The second feature is that instead of

the clinical Medtronic Activa IPG you will have a research, next generation IPG implanted (Medtronic Summit RC+S) device, which allows both the dual electrode stimulation and the adaptive mode of DBS stimulation. By having this research IPG device implanted, you can receive both standard clinically effective stimulation but also be a research subject for new types of stimulation protocols. The expectation is that you would return for research periods (a day at a time) to test these various modes of possibly improved stimulation to see if they are better than standard clinical single-site stimulation. This type of long-term research cannot be performed by the currently available Food and Drug Administration (FDA) approved Medtronic Activa IPG. By gaining an understanding of how brain activity and movement disorder symptoms are related, we can better understand how deep brain stimulation treats movement disorders and help to design the next generation IPG devices.

During your planned surgery, the research will test electrical recordings obtained by the dual electrodes in your brain, and you will be tested for treatment of your movement disorder symptoms. This study will involve two different treatment electrodes on each side of your brain for comparison of which is clinically optimal and for recording responses between the two electrodes. Temporary extension wires will be attached to your deep brain stimulation system and connected to a research stimulator. Over the next 45 minutes we will change the stimulation settings and measure the effects on your brain activity and movement disorder symptoms, using the Duke recording system developed by Dr. Grill and/or a non-implantable version of the Medtronic recording system, termed Summit RC+S. You may be asked to raise your arm for short intervals while measurements of your tremor are recorded. Additionally, you may be asked to press alternately the right and left buttons of a computer mouse with your index and middle finger for short intervals to measure your bradykinesia (slowness of movement). Further, you may be asked to rate any side effects that you feel during stimulation. After completion of the intraoperative phase of the research, the temporary external extension wires will be removed and we will proceed with the remainder of the planned deep brain stimulation implantation surgery. A representative of the medical device company that manufactures your deep brain stimulator may be present during surgery, but this person will not participate in the conduct of the research.

Brain imaging procedures will be performed before [Magnetic Resonance Imaging (MRI) scans] and after [Computerized Tomography (CT) scans] your operation as part of the standard procedure for DBS implant surgery and post-operative follow-up. Your participation in the research study will not alter these procedures, but the study team may use the images to determine the location of the DBS electrodes in your brain.

After the DBS electrodes are placed in your brain during either one or two sessions, depending on how well you tolerate the surgery, you will be in the hospital under observation at least overnight, which is standard clinical practice. As part of this study, your overnight observation will take place in the ICU (intensive care unit) so you can be watched carefully for any problems that may arise. After you are discharged, during a subsequent outpatient operation, you will have the research IPG (Medtronic RC+S) implanted in your chest area, which will be connected to the DBS leads in your brain through wires running behind your ear. Research to test electrical recordings in your brain will also be done during

this IPG implant surgery. Before the IPG is implanted, temporary extension wires will again be attached to the deep brain electrodes that were implanted in your prior surgery and connected to a research stimulator. Over the next 45 minutes we will change the stimulation settings and measure the effects on your brain activity, using the Duke recording system and/or a non-implantable version of the Medtronic recording system. These electrical recordings will be compared to the electrical recordings made during your prior DBS electrode implant surgery.

After completion of the intraoperative phase of the research, the temporary external extension wires will be removed and we will proceed with the remainder of the planned IPG implantation surgery. A representative of the medical device company that manufactures your deep brain stimulator may be present during surgery, but this person will not participate in the conduct of the research.

Staging the surgeries to implant the DBS electrodes and IPG at different times is a standard, clinical approach since it is better tolerated by patients. Since you will be obtaining the standard clinically-expected DBS benefit (or potentially more benefit) as a research subject, all clinical care costs will be the same as for any DBS procedure, covered by your insurance company.

As with any DBS procedure, you will need to return to the Neurosurgery and Neurology clinics to adjust the DBS device to obtain the best clinical effects, typically over 3-6 months, which is the clinical standard of care. Because there are two electrodes placed on each side of your brain this adjustment may take longer since each electrode has to be adjusted separately, then compared between the two electrodes. These visits will involve being off medications overnight, and UPDRS studies will be performed, similar to those performed per standard of care prior to surgery. Once both electrodes are fully adjusted and the optimal clinical benefit obtained (as with any DBS procedure), then we will test your Parkinson's disease outcome using the Hauser diary, UPDRS testing both on and off medications, and the PDQ-39 scale. These are standard clinical programming visits to determine the best treatment effect, covered by your insurance company. These adjustments or programming require a research device [Summit Research Lab Programmer (RLP)] that is not widely available in the USA so any further adjustments may require returning to Duke University for these adjustments.

After this initial part of the study shows which combination of electrodes gives you the best stimulation, then you will be treated with this stimulation format on a continuous basis to obtain the standard expected clinical efficacy. The Summit RC+S is rechargeable so you will need to recharge the device every 1-3 days as needed. There is no equivalent non-rechargeable device available so the recharging procedure is important to maintain the clinical function of the device. There is a burden of extra time involved for having to recharge the device occasionally so this extra burden is important to consider. It will be important that either you (the subject) or the caregiver be able to recharge the IPG as needed.

After this clinical programming phase we will invite you back to Duke University for day-long research visits (i.e., 6-8 hours), to start testing your function with adaptive stimulation. This involves measuring signals in the brain through the RC+S device to either turn the stimulation on or off intermittently

(automatically) or to turn the stimulation slowly up and down automatically. We will try multiple different settings on both the same day and different days over time, to test whether the adjustable stimulation settings give you better improvement in your Parkinson's symptoms or fewer side effects or allow the RC+S device to go longer between charging. We may also measure your brain signals using an electroencephalogram (EEG). An EEG records your brain activity using temporary, small metal sensors (electrodes) that are placed on your head with gel. This recording does not hurt and the electrodes will be removed at the end of the day.

It is expected that you will return at least one day a month to test these research settings, for the duration of the research period (i.e., up to 4 years, and potentially longer if an extension can be funded and you are doing well). If any of the research settings consistently improve your clinical benefit, then we may leave you on the research settings between visits as well.

We will also assess your Parkinson's symptoms and compare them to your pre-operative symptoms. These assessments will be performed at least once a year throughout the length of the study. We may also measure signals in your brain using your implanted RC+S device while you are completing these assessments.

You will also complete some study activities at home in place of or in addition to the day-long research visits at the clinic. One of these activities will be recording the signals from your RC+S device as you go about your normal daily activities. This allows us to see how your brain signals change depending on the type of activity you are doing, such as walking, sitting, or sleeping. We will provide you with a tablet computer and a communicator device that is able to read the signals from your RC+S and automatically save them to the tablet. The tablet device is meant to run on remote control from our computers at Duke. We will also provide an iPhone and Apple Watch which will allow you to log your Parkinson's medication and record your symptoms. We will set up this equipment for you and teach you how it works and help to upgrade your home WiFi to a suitable level if needed.

We will also ask you to participate in remote study visits on a videoconference (such as Zoom). We will plan these with you to accommodate your schedule, up to 4-5 hours per week, but only 1-2 hours at a time. Using the tablet computer and communicator device you use for home recordings, we will be able to adjust your DBS settings to test adaptive stimulation, similar to what we do at the day-long research visits at Duke University. Since we want to be able to see how you respond to each setting and make sure you don't have any side effects, we will only make these stimulation adjustments when we can see you over videoconference. We will provide you with an iPhone for videoconferencing. We will also set up this iPhone for you and teach you how it works. We expect to have a video visit every week if possible. We will schedule these visits with you in advance to find a time that is convenient for you. During these videoconferences, we will also download any data you recorded at home during your normal daily activities.

If at any time you do not like one of the adaptive stimulation settings, you can always return to your preferred clinical program by using your home programmer.

At the end of the study, we will collect the tablet computer, iPhone, Apple Watch, communicator device, and any other study equipment we provide for remote visits.

HOW LONG WILL I BE IN THIS STUDY?

Your participation in this study will last up to 4 years. At the end of that time, you may be able to continue with the optimal clinical stimulation pattern that has been set for you, since the rechargeable RC+S device can last up to 9 years before needing to be replaced. However, since this is a research device, it will need to be eventually replaced with a standard clinical device that is available at the time of replacement.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first. You will still need to be followed clinically for the DBS settings and if you do not want to participate in the research you can either keep the research IPG or have a small surgery to have a standard clinical IPG implanted (i.e., Medtronic Activa). However, if a standard IPG is implanted only one electrode on each side can be connected, so you may lose some of the benefit from either dual electrode stimulation or from adaptive stimulation; neither of these advanced forms of DBS stimulation can be performed with the regular DBS IPG. If returning for the research visits becomes a problem, we can adjust the visits as needed to be able to continue the research if possible.

Research staff will have access to review your medical records periodically until study closure.

WHAT ARE THE RISKS OF THE STUDY?

There is a small risk of infection associated with connecting your deep brain stimulation electrodes to the external pulse generator and recording system during the two surgeries to implant the deep brain stimulation system (3.5-4% total risk). After the electrodes have been implanted through a small burr hole in your skull during the lead implant surgery, a temporary wire will be used to connect your electrodes to the research system in the operating room and we will do intraoperative research for approximately 45 minutes. Similarly, during the surgery to implant your IPG, after implanting the extension wires that connect your deep brain electrodes to the IPG, a temporary wire will be used to connect the extensions to the research system in the operating room and we will do intraoperative research for approximately 45 minutes. This additional research time during the two surgeries increases the risk of infection, but this risk is minimized because the wire will remain in a sterile area during the experiments. Additionally, there is a small additional risk of bleeding into the brain (hemorrhage) from placing a second treatment electrode into a standard region of the brain used to treat Parkinson's disease.

Risks of all DBS procedures include this risk of infection from having electrodes and an IPG implanted (~3.5%), risks to the brain of placing the electrodes (~ 3% for both sides) and long-term risks of wiring

malfunction. Because this study involves two additional electrodes there is a slightly increased risk of infection (i.e., up to ~ 4.0%) and brain hemorrhage/stroke issues, slightly higher than the typical single-site DBS (i.e., ~ 4.0% vs the single site risk of 3.0%). If you are concerned about this small additional risk, you can choose to have two electrodes placed on only one side of your brain, and just one electrode placed on the other side of your brain. If you choose to do this, the side of your brain that has two electrodes would typically control the side of your body with the worst symptoms. Because this study involves two additional electrodes, more wires are needed to connect the electrodes to the IPG. This causes a slightly higher risk of scarring around the wires resulting in needing another surgery to correct it or other wiring malfunction.

The Medtronic Summit RC+S IPG and the associated programmer (Summit RLP) are both research systems and there may be risks involved with using a research system that are currently unknown, compared to a standard clinical device. This device is not MRI-compatible so it is unsafe to proceed with an MRI scan anywhere in the body.

You will be asked to not take your anti-tremor and/or dopaminergic medications 12 hours before your surgery and during some of the DBS adjustments and tests after the procedure. Not taking these medications creates risks associated with the symptoms you experience in the OFF medication state. You should discuss these risks with your physician. This is a standard clinical aspect of the deep brain stimulation implant procedure.

Some stimulation settings may cause side effects or worsen symptoms, causing discomfort. As soon as the stimulation is turned off, any side effects of the stimulation will stop. The side effects that you might experience include sensations of numbness and tingling, muscle contractions, and difficulty speaking. You will be asked to report any sensations that you feel as a result of the stimulation and you will be observed for any effects of the stimulation on your motor symptoms.

There is a slight risk of electrical shock or tissue damage at the deep brain stimulation electrode due to connection to the equipment required to conduct the intraoperative study. The strength of the electrical stimulation will not exceed the manufacturer's recommended limit. The safety of the complete electrical set up will be tested and documented before any testing is done. Periodic biomedical safety checks will be performed for the intended use of all electromechanical equipment used during these intraoperative studies.

No general anesthesia will be given to you during surgery to implant the deep brain stimulation electrodes. You will receive monitored anesthesia care and will be administered sedatives as needed. The procedure will be mostly performed under local anesthesia (injection of numbing medicine in the area of your head where the skin is cut for electrode implantation) to allow you to perform the tasks required for clinical localization of the electrodes, as routinely performed for DBS electrode placement. This can cause minor discomfort or anxiety in some subjects. However, general anesthesia is used to perform the IPG implantation in the chest since this cannot be performed under local anesthesia.

There are risks associated with undergoing brain imaging procedures required for DBS implant surgery and post-operative follow-up. Your participation in this study does not modify these procedures or their associated risks. After surgery only CT scans are allowed.

Since undergoing an elective procedure may have some risks to pregnancy we do not perform any DBS procedures during pregnancy. If at the time of pre-operative screening you are found to be pregnant (usually confirmed by a pregnancy test) then the elective DBS procedure you are planning to undergo will be canceled and no research will be conducted. The planned DBS procedure would normally be rescheduled after conclusion of the pregnancy when the conditions are safer.

There is a risk that the tablet computer and iPhone you use for home recording and videoconferencing could be hacked. We have set them up with data security in mind using Duke IT's protocols. Such measures include encrypting the hard drives and requiring a password to unlock the devices. However, these measures are defeated if you share your username and password. We will contact you via telephone or video conference before attempting to access the tablet, so do not accept unexpected connection requests.

There may be risks, discomforts, or side effects that are not yet known since this is a research study using a research device.

If side effects occur that do not stop when stimulation is turned off or if other problems arise, you should report them immediately to one of the following clinical investigators: Dennis A. Turner, MA, MD, Department of Neurosurgery, Jeffrey Cooney, MD, Department of Neurology, Kyle Mitchell, MD, Department of Neurology, or Shivanand (Nandan) Lad, MD, PhD, Department of Neurosurgery, all available on page at 919-684-8111, so that you can be properly treated. In the event of a medical emergency, please dial 911.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
There may be direct benefit to you from being involved with testing novel forms of DBS stimulation, including dual electrode stimulation and adaptive stimulation. In addition to receiving the expected, clinical benefit from the DBS system the use of dual electrodes on each side of the brain may allow improved stimulation, with either fewer side effects or more benefits. The novel, adaptive mode of DBS stimulation may also show improved clinical benefits compared to standard clinical, single-site DBS stimulation. The results of this study will be used to understand better how deep brain stimulation treats the symptoms of movement disorders and to investigate the use of electrical signals generated in the brain to select stimulation settings more efficiently and effectively for the next generation of deep brain stimulation devices.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?
Instead of being in this study, you have the following alternatives:

- You can choose to have standard DBS surgery. Standard DBS surgery involves implanting a single electrode on each side of your brain (or just one side of your brain, depending on your symptoms) and implanting a standard, FDA-approved IPG.
- You can choose not to have surgery and continue treating your Parkinson's Disease symptoms medically.

Please talk to your doctor about these and perhaps other options.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed and/or used for study-related activities by individuals involved in this research and by those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

Since the Medtronic Summit RC+S is an investigational device, all device information and data will be shared with Medtronic. This sharing will allow rapid evaluation of any device problems and device performance.

The data you send to us from home recordings and home video visits will be processed by a company called Rune Labs. Rune Labs is a company set up to process the large amounts of data that are recorded from the RC+S device. Part of their service is to remove information that could identify you from this data before it is analyzed. Duke University has negotiated with Rune Labs for this processing and to make sure the data stays as safe as possible.

In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration, representatives of the National Institutes of Health, and the Duke University Health System Institutional Review Board. If your research record is reviewed by any of these groups, they may also need to review your entire medical record. If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by the federal privacy regulations.

The Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);

2) you have consented to the disclosure, including for your medical treatment; or

3) the research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the FDA.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

The study results will be retained in your research record for at least six years after the study is completed. At that time either the research information not already in your medical record will be destroyed or information identifying you will be removed from such study results at Duke University Health System (DUHS). Any research information in your medical record will be kept indefinitely.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your identity will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

WHAT ARE THE COSTS?

There will be no additional costs to you as a result of being in this study. You or your insurance provider will be responsible and billed for all costs related to your routine medical care, including copayments and deductibles. Routine medical care services are those that you would have received for your condition if you were not participating in this research study. Not all services are covered by insurance. Some procedures or scans may require pre-authorization by your insurance plan. We will notify you if we learn that a service is not covered by your insurance plan as part of the pre-authorization process. If it is not covered, you will be responsible for paying for it. The amount of your out-of-pocket expense will depend on your insurance plan. For beneficiaries with Medicare Advantage

Plans, traditional Medicare is billed for the routine cost of a research study. You may have more or higher co-pays than with a Medicare Advantage plan. Please discuss the costs of the study with Dr. Dennis A. Turner. At your request, a Financial Counselor in the clinic may provide you with an estimate of costs for routine services.

All of the research visits for testing novel modes of stimulation will be paid for by the research study, but clinical programming visits will be paid for by your regular insurance since you will be receiving the standard clinical expected benefit from DBS stimulation, and these visits are required to be able to perform this programming.

The research IPG (Summit Medtronic RC+S) is being provided by Medtronic free of charge.

There is a possibility that at the end of the currently funded study (up to 4 years) this research device will no longer be supported, and you may be required to have the battery (IPG) replaced surgically with a standard, clinically-available DBS device at that time instead.

WHAT ABOUT COMPENSATION?
You will receive $500 for each full research day that you return to Duke University and undergo research stimulation (or $250 if you only participate for a half-day), up to 12 visits per year. In addition, we will reimburse you for travel to and from Duke University.

You will receive $25 per hour for each videoconference visit where you undergo research stimulation, up to 120 hours per year.

You will receive $2.50 for each 8-hour block of home recordings of your daily activities you submit.

You will receive $50 per hour for the yearly assessment of your Parkinson's disease symptoms. In addition, we will reimburse you for travel to and from Duke University.

The maximum amount of compensation and travel reimbursement for all study activities is $12,000 per year.

Payment received as compensation for participation in research is considered taxable income to you, the research subject. If payment to an individual exceeds $600 in any one calendar year, Duke University is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of Duke University exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to you and a copy sent to the IRS.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by

DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
Scalar Closed-Loop STN/GPi DBS Based on Evoked and Spontaneous Potentials (Permanently Implanted Medtronic RC+S Studies)

Duke University, Duke University Health System, Inc., your Duke physicians, or Medtronic, to provide monetary compensation or free medical care to you in the event of a study-related injury. The research IPG (Summit Medtronic RC+S) is being provided by Medtronic Neurological free of charge.
When the device system reaches its end-of-life (at around 9 years) or needs to be removed for any reason, you may choose to receive a standard clinical device as a replacement. The cost for any replacement is the responsibility of you or your insurance provider, including the surgical costs.

For questions about the study or research-related injury, contact Dr. Dennis A. Turner at (919) 684-6706 during regular business hours and at (919) 684-8111 after hours and on weekends and holidays. Further information concerning this and your rights as a research subject can be obtained from the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

Study staff may review and record your medical records following completion of the study to monitor for study-related complications. Any recordings of complications or adverse events (a bad effect) that occurred following participation in the study will be keep confidential and will be destroyed within six years of your participation in the study.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?
You may choose to decline participation in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event related to the study. However, as long as you have the Medtronic Summit RC+S research IPG implanted Medtronic will continue to collect information on this device, as required by the FDA. If an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled and will not affect your access to health care at Duke. If you decide to withdraw from this study, we ask that you contact Dr. Turner in writing and let him know that you are withdrawing from the study. His mailing address is: Duke University, Department of Neurosurgery, Box 3807, Durham, NC 27708-0281.

If you withdraw from the study then the Medtronic Summit RC+S research IPG may need to be removed and replaced with a standard clinic IPG (i.e., Medtronic Activa device). However, only one electrode on each side can be connected to this clinical IPG, and the device is not capable of adaptive stimulation. Thus, if you withdraw and elect to have the research device removed you may lose some of the benefits from this advanced research device. You will be asked to meet with Dr. Turner for a study exit visit to discuss your options.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, you have serious side effects, or your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. If this occurs, you will be notified and your study doctor will discuss other options with you. You will not be required to complete any follow-up treatments or assessments for research purposes if you withdraw from the study.

Your data may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your data, we will no longer be able to identify and destroy them.

A description of this research study 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.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, contact Dr. Turner at (919) 684- 6706 or Dr. Lad at (919) 970-6850 during regular business hours and by pager at (919) 684-8111 (Turner or Lad) after hours and on weekends and holidays.

If you have problems, concerns, questions or suggestions about the research, contact Dr. Turner at (919) 684-6706 during regular business hours and at (919) 684-8111 after hours and on weekends and holidays.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

THIS SECTION INTENTIONALLY LEFT BLANK

DUKE UNIVERSITY HEALTH SYSTEM

Consent To Participate In A Research Study
Scalar Closed-Loop STN/GPi DBS Based on Evoked and Spontaneous Potentials (Permanently Implanted Medtronic RC+S Studies)

STATEMENT OF CONSENT

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time
_____	_____	_____
Signature of Witness (if applicable)	Date	Time