Northwell Health

Campus: Zucker Hillside Hospital

Consent for Participation in a Research Study

Study Title: Reclaim™ Deep Brain Stimulation (DBS) Therapy for Obsessive-Compulsive Disorder (OCD)

Principal Investigator: Albert Fenoy, MD

Sponsor: Northwell Health, Zucker Hillside Hospital, Feinstein Institutes for Medical Research

About this research
You are being asked to participate in a research study.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Important Information
This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

Why am I being asked to provide my consent?	This is a research study, which is different than personal medical care. Scientists do research to answer important questions which might help change or improve the way we do things in the future.
Do I have to join this research study?	No. Taking part in this research study is voluntary. You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled.
Why is this research study being done?	The purpose of this study is to demonstrate the feasibility and safety of performing bilateral stimulation of the anterior limb of the internal capsule deep brain stimulation (DBS) as a treatment for treatment resistant obsessive-compulsive disorder (OCD).
What will happen to me during the study?	If you agree to participate, you will undergo surgery for implantation of the deep brain stimulation device.
How long will I participate?	The study includes 15 study visits. Visits will occur after 2 weeks, 1, 2, 3, 4, 6 months and then every 6 months for 60 months. The study will be for approximately 5 years.
Will taking part expose me to risks?	The major risks to patients are related to device implantation. Implanting the DBS system from Medtronic carries the same risks associated with any other brain surgery. The other major risk is associated with the DBS itself. There

	is a risk that DBS may lead to an increase in suicidal ideation (thoughts of death or killing oneself). **Possible common side effects of brain stimulation include:** Changes in mood (positive and negative); Diplopia (double vision); Gastrointestinal disturbances (changes indigestion) or nausea; and, Tingling sensation (paresthesia). A complete list of possible risks and side effects can be found below in the detailed risk section. The complete list of possible side effects and risks of the procedures can be found below in the detailed risk section of this consent form.
Are there any benefits to participation?	Specific benefits to the subject include a potential improvement in clinical symptoms.
What are my alternatives to participation?	Alternative procedures or courses of treatment would be standard care.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether to participate in this research.

Introduction
You are being asked to join a research study. The purpose of a research study is to answer specific questions, sometimes about the safety of a drug or device and how well it works. Being in a research study is different from being a patient. When you are a patient, you and your doctor have freedom in making decisions about your healthcare. When you are in a research study, the researcher will follow the rules of the research study as closely as possible, while monitoring your health.

You do not have to be in this study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the study.

Financial Disclosure: Albert Fenoy, MD is a consultant for Medtronic. There is a financial interest held by Dr. Fenoy that could be affected by the results of the study. This disclosure is made so that you can decide if this relationship may affect your willingness to participate in this study. You are not under any obligation to participate. If you have any questions, please ask the researcher or a member of the research team.

Why is this research study being done?
The purpose of this research study is to perform deep brain stimulation (DBS) in treatment resistant obsessive-compulsive disorder (OCD) patients targeting the anterior limb of the internal capsule. Specifically, this investigation will assess the efficacy and safety of DBS in treatment resistant OCD and analyze the incurred changes in brain function.

Why is this research?
Definition of a Humanitarian Use Device

In February 2009, the Food and Drug Administration (FDA) gave approval of a Humanitarian Device Exemption (HDE) of a Humanitarian Use Device (HUD) for Medtronic Reclaim Therapy to Medtronic, Inc.

Humanitarian use devices are medical devices approved by the FDA for the treatment of medical conditions affecting fewer than 4,000 patients per year. In granting HDE approval for a humanitarian use device, the FDA focuses primarily on the safety of the device, rather than how well it helps. Although there is evidence that suggests the use of the Reclaim Therapy probably helps patients' symptoms, the FDA's HDE approval indicates that the helpfulness of this therapy has not been proven.

The Medtronic Reclaim DBS Therapy is indicated for (meant to be used for) bilateral stimulation of the anterior limb of the internal capsule (a specific location in the brain) used along with your medications and as an alternative to anterior capsulotomy (a different type of brain surgery) for treatment of chronic, severe, treatment resistant OCD in adult patients who have failed at least three selective serotonin reuptake inhibitor (SSRI) medications.

You are being asked to participate in this study because you have OCD and have not responded to previous treatments.

How many people will take part in this study?
This research study hopes to enroll 20 people.

How long will you be in this study?
The study includes 16 study visits, each lasting around 30 minutes. Visits will occur after 2 weeks, 1, 2, 3, 4, 6 months and then every 6 months for 60 months. The study will be for approximately 5 years.

What will happen in this research study?
Your doctor will decide if one or two neurostimulator systems are needed to control your symptoms. If two systems are required, your doctor will need to place the neurostimulators at least 8 inches apart to assure they can each be properly programmed. Your doctor may place the neurostimulators either near your collarbones, within your abdomen, or both as needed to allow the proper distance between the neurostimulators.

The evening before surgery, you may be instructed to stop taking all of your medications. This is so the effect of the Reclaim Therapy on your symptoms can best be determined. You will be admitted to the hospital either the night before or the morning of your surgery. You may have your head shaved prior to surgery to help prevent infection.

The day of surgery, the following steps may occur:

1. A metal frame will be attached to your head. The frame is a special instrument that allows your surgeon to find the correct path to the target site in your brain.

2. Pictures of your brain will be taken using MRI (magnetic resonance imaging) and/or computer-aided tomography (CAT) scans. This will allow your surgeon to determine the area in your brain where the leads will be placed.
3. You will then go to the operating room where a small hole will be drilled in your skull for each system. You will receive local anesthesia before this procedure. This hole is needed to place the lead in your brain.
4. Later in the surgery, a cap will be placed over this hole. Your surgeon will test stimulate areas of your brain to determine the best placement for the lead.
5. When the best target in the brain is located, the lead is then passed into the brain. The control of your symptoms will be checked again. The lead's position is then held in place with a cap in the hole in your skull.
6. The metal frame is then removed from your head. If you do not have the extension and the neurostimulator implanted right away, you will typically be allowed to go home in about 24-48 hours. Your doctor will decide the length of your hospital stay.
7. At the time the extension and neurostimulator implanted are implanted, you will then be sedated and asleep under general anesthesia. You will typically be allowed to go home in approximately 24-48 hours. Your doctor will decide the length of your hospital stay.

Follow Up Schedule
Your physician will want to see you for follow-up after surgery. Two kinds of follow-up visits will be scheduled: Dr. Fenoy will follow-up with you regarding surgery, and Dr. Argyelan will follow-up regarding improvement in your OCD symptoms. Weekly follow-up visits might be needed after surgery for 4-6 weeks. After that, you will be seen based on your doctors' recommendations. Your doctors will schedule you according to your individual circumstances. It is important that you do not skip these appointments. You will participate in this study and follow up with us for one year; at that point, you can choose to follow up on a more periodic schedule.

You may not experience immediate symptom suppression from the therapy. Frequent, non-invasive adjustment to the stimulation parameters may be required to achieve optimal symptom suppression. This adjustment period may take weeks or months and will be done during the follow-up visits.

Deep Brain Stimulation Device
Implantation of all devices will be performed at a single surgery, as described above. DBS electrode implantation will take place under local anesthesia, after a head frame is placed on your head. Two electrodes, one for the left-sided and one for the right-sided target in the brain, will be placed through holes drilled in your skull. Each will be fixed to the skull using a plastic securing device covering the hole through which it was drilled.

Once these are secured, you will be placed under general anesthesia, where two extension wires (one for each DBS electrode) will pass from the scalp area under skin to below your collarbone in your chest, where a battery will be placed. You will then be sent to recovery room after you wake up, and then admitted to the hospital where you will stay overnight. You would then most likely go home the next day only after the neurosurgery team see that you are able to do so.

Before you go home, you will have a CT to check for bleeding and a MRI performed to verify electrode placement.

MRI machines use a strong magnet to make pictures of the inside of your body. During the scanning, you will lie on a long narrow couch for 1 hour while the machine gathers data. You will not feel anything while the data is being collected. You will also hear tapping noises that are from the MRI scanner.

Since the MRI scanner is a magnet, metal objects will be attracted to the scanner. It is very important that you tell the researcher about any metal objects, devices or implants that are in or on your body before you enter the scanner room. All metal objects must be removed before entering the magnet room. In some cases, having those devices may mean that you should not have an MRI scan.

What are the risks of the research study? What could go wrong?

Possible Device Complications

You will sign a consent form on the day of surgery at North Shore University Hospital for these risks. Thus, risks of brain surgery include bleeding, infection, stroke, paralysis, death. The PI has performed over 700 such DBS procedures so as to minimize the chance of these risks.

Explantation of the DBS system and revision of DBS electrodes carries the same risks as implantation of DBS lead electrode system. Revision/replacement of pulse generator risks include hemorrhage or infection. There is additional surgical risk associated with pulse generator replacements; the maximum lifetime of the Percept PC battery is longer than 5 years, but actual duration is dependent on stimulation parameters. Since both leads are powered from one battery, sometimes replacement of the extension wires is required to make the proper connection to the new battery system. The extension wires are attached to the intracranial electrodes within the scalp. The proximal connection of the old extension wires to the intracranial electrodes must be undone, and new extension wires need to be attached and tunneled down to the battery location. There is a less than 5% chance that this revision may result in damage to the intracranial electrodes, which would then require additional surgery to replace them. In the worst-case scenario, this would delay therapy and incur all the risk of intracranial electrode placement. Usually, what this extra step would mean is that there is an additional incision at the scalp in addition to the incision at the battery site, and there is a small risk that, relative to the usual replacement surgery, the scalp site would also be at risk for infection.

- There may be pain, lack of healing, or infection where the DBS parts are implanted.
- The DBS parts may erode through skin, which can cause an infection or scarring.
- The lead or lead/extension connector may move, requiring surgical re-adjustment.
- Components or parts of the DBS system may break or fail to work properly, requiring surgical repair or replacement.
- Stimulation could stop because of mechanical or electrical problems. Either of these would require surgery. The DBS implanted pulse generator (IPG) service life depends on individual use. The DBS PG service life for tremor typically ranges from 2-3 years.

- An allergic reaction to the DBS system may occur. The DBS system materials coming in contact with tissue include titanium, polyurethane, silicone, and nylon. Also, the body could reject the system (as a foreign body).
- There is the possibility of tissue damage resulting from the programming parameters or a malfunction of one of the parts of the DBS system.

Risks of Surgery
Implanting the neurostimulator system carries the same risks associated with any other brain surgery. Risks may include:

- Paralysis, coma, and/or death
- Bleeding inside the brain (stroke)
- Leaking of fluid surrounding the brain
- Seizures
- Infection
- Allergic response to implanted materials
- Temporary or permanent neurological complications
- Confusion or attention problems
- Pain at the surgery sites
- Headache

Possible Side Effects
Side effects of brain stimulation may include the following:

- Suicidal ideation (thoughts of death or killing oneself)
- Depression (feeling sad, down, or blue, and/or a loss of interest in things usually enjoyed)
- Increased OCD symptoms/fluctuating results
- Changes in mood (positive and negative)
- Gastrointestinal disturbances (changes in digestion) or nausea
- Tingling sensation (paresthesia)
- Dizziness or lightheadedness (disequilibrium)
- Facial and limb muscle weakness or partial paralysis (paresis)
- Facial flushing (red or rosy facial color) or facial muscle contractions
- Jolting or shocking sensation
- Numbness (hypoesthesia)
- Increased heart rate
- Hyperactivity or euphoria (hypomania)
- Pain or discomfort
- Headaches
- Dry mouth
- Itching at the surgical site(s)
- Insomnia
- Increased fatigue (feeling exhausted or moving slower than usual)
- Cognitive disturbance (“cloudy” thinking)

- Restlessness
- Weight gain or weight loss

General Anesthesia
There are always risks with general anesthesia. This may include a reaction to medications you receive, heart attack, or even death. A tube will be placed in your mouth to help with your breathing while you receive general anesthesia. There may be unknown risks.

Your doctor should carefully monitor you for behavior changes. Such symptoms may include changes in sleep or eating behavior, irritability, disinhibition (unrestrained behavior), anger, aggression, and a predisposition to accidents. Most of the stimulation side effects can be avoided by reprogramming the neurostimulator or turning the neurostimulator off. Other side effects or complications may occur which are more unusual or are not yet known and cannot be predicted at this time. The lead will remain implanted indefinitely unless a problem necessitates removal. The neurostimulator may need to be replaced every six to 16 months as the battery depletes. Sudden or expected (abrupt) discontinuation of stimulation for any reason should be avoided as it may cause a return or worsening (i.e., "rebound" effect) of disease symptoms.

Magnetic Resonance Imaging (MRI) Studies
The magnetic resonance imaging (MRI) machine is a powerful magnet. It is very important that you tell the researcher about any metal objects, devices or implants that are in or on your body before you enter the scanner room. All metal objects must be removed before entering the magnet room. In some cases, having those devices may mean that you should not have an MRI scan. If you know of any metal in your body, you will need to tell the researcher right away. Otherwise, there are no known risks of MRI. Some people with claustrophobia (fear of closed spaces) may find the MRI scanner too confining. In that case, you can ask to be removed from the scanner and this will be done immediately. The MRI scanner makes a loud beeping sound. We may ask you to wear protective earplugs during scanning. In addition, a gel marker will be placed on your head during the scan. These markers are routinely used and are MRI compatible. Because these markers are attached to the side of the head, they may cause slight skin irritation. On rare occasions, some subjects may experience one or more of the following: momentary dizziness, nausea, tingling sensations and/or muscle twitches. Please tell the investigator over the intercom if any of these sensations occur.

All scans are reviewed by a radiologist. If the radiologist thinks there might be a problem or the scan reveals a condition that could affect your health, you will be referred for the proper follow-up care to your primary care physician or another specialist. This MRI is not the same as one that your own doctor would order. It may or may not show problems that would be found on a standard MRI.

During the MRI, you may experience heating due to your implanted device, or an unusual sensation due to unintended stimulation. This is highly unlikely. If this does occur, please squeeze the call button in the MRI machine or tell the technician immediately and the MRI will be stopped.

Incidental Findings

Although the imaging you will have in this study is being undertaken for research purposes only, it is possible that doctors may notice something that could be important to your health. Although not likely, it is possible that the doctors may notice something that may be very serious and could immediately affect your life. If so, we will contact you to explain what was observed. If you so desire, we will also talk with your private physician. If you do not have a private physician, we will refer you to an appropriate clinic for follow-up. It will be your choice whether to proceed with additional tests and/or treatments to evaluate what we observed, and you or your insurer will be responsible for these costs.

Collection of Sensitive Information
Some of the questions we will ask you are personal. You may feel embarrassed or stressed. You may ask to see the questions before deciding whether or not to take part in this study.

Unknown Side Effects
As with any device, there might be side effects that are unknown at this time. You will be closely watched for side effects. You should report any unusual events to the study staff.

Interviews/questionnaires/QOL assessments that discuss sensitive issues that may cause <u>emotional upset</u>, such as grieving:

Some of these questions may seem very personal or embarrassing. They may upset you. You may skip any question that you do not want to answer. If the questions make you very upset, we will help you to find a counselor.

Risks to Women of Childbearing Potential and Pregnant Women
We do not know the effects of DBS on fertility or a fetus. For this reason, if you believe you are pregnant or have a chance of becoming pregnant, you should not take part in this study. A urine pregnancy test will be performed prior to the start of study procedures. If you are pregnant, you will not be allowed to be in the study.

If you do take part in this study, you must use a medically recognized form of birth control for one month before entering the study, while in the study, and for at least one menstrual cycle after stopping the study. If you become pregnant during the study, you will be immediately withdrawn from the study and closely monitored through your entire pregnancy.

The side effects of this experimental procedure on newborns are also not known; therefore, if you are currently breastfeeding you cannot be in this study.

What are the benefits of this research study?
You may or may not benefit from this procedure. The benefits we hope you receive is that it would improve your symptoms of obsessive-compulsive disorder.

Reclaim Therapy may help you manage your symptoms, but it is not a cure. Significant OCD symptoms are likely to persist following Reclaim Therapy. When you turn on the brain stimulation system, it will deliver stimulation that may decrease some of your symptoms. The

stimulation may also make it easier for you to engage in cognitive behavior therapy (CBT), which may also help control your symptoms. Your symptoms will probably return when the system is turned off.

Will I receive my results?
We may learn things about you from the study activities which could be important to your health or to your treatment; however, we will not share this information with you because the results are research related and cannot be used for treatment without established confirmatory testing.

If you do not want to take part in this research study, what are your other choices?
If you do not join this study, you have other choices for treatment. Talk to your doctor about your choices. Your other choices may include:

- Another research treatment
- Standard treatment
- No treatment
- Treatment provided on this study

Your doctor can also tell you the important risks and benefits associated with the alternative treatment.

Are there any costs for being in this research study?
The participant or his/her insurance carrier will be responsible for the tests, procedures, etc. of the study. Taking part in the study may lead to increased costs to the participant or his insurance company.

Will you receive any payments for participating in this research study?
Participants do not receive any payments or compensation for participating in this research study.

What happens if you are injured while participating in this study?
If you are hurt from being in the study, you will receive medical care and treatment as needed from Northwell Health. However, you will be responsible for the costs of such medical treatment, directly or through your medical insurance or other forms of medical coverage. Northwell Health is not offering to provide you the drug/device after the termination of the study or to pay you for pain, worry, lost income, the cost of your medical care or non-medical care costs that might occur as a result of your taking part in the study. However, you do not waive any of your legal rights by signing this form.

Wording for Industry-Sponsored Studies
If you are injured or harmed as a result of participating in the study and receive medical care through Northwell Health or any other health provider, you will be sent a bill for whatever medical care you receive. All or part of your bill may be paid by your medical insurance or other forms of medical coverage. In general, the study sponsor may pay these providers for any reasonable medical expenses to treat your injury. The study sponsor, however, is not offering to pay for medical expenses that are covered by your insurance provider or if your injury was not caused by the study drug/device or a study procedure. Northwell Health is not offering to provide you the drug/device after the termination of the study or to pay you for pain, worry, lost

income, the cost of your medical care or non-medical care costs that might occur as a result of your taking part in the study. However, you do not waive any of your legal rights by signing this form.".

What are your rights as a research participant?
Your participation in this project is voluntary. The quality of your medical care will be the same, whether you join, refuse to join, or decide to leave the study.

If you do not join the study you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time without prejudice to your future care at Northwell Health. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?
It is also possible that your participation in this study may end without your consent. This decision may be made by a researcher, study sponsor or the Institutional Review Board (IRB- the committee that oversees research at this institution).

Reasons for withdrawal may include:

- failure to follow instructions,
- failure to show up for study visits,
- it is not in your best interest to continue on this study, or
- the study is stopped.

If you withdraw from this study or if you are withdrawn from the study, any data (or samples) already collected will continue to be used. However, no new data will be collected.

What happens if new information is learned?
You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part in this study may be obtained again.

What will happen with the information we collect as part of this research study?
Any study information about you will be kept private and will only be given out with your permission. If the results of this study are published, your name will not be used. Your research records will be private to the extent allowed by law. In order to make sure the research is done properly, the Human Research Protection Program (a group of people that oversees research at this institution) may need access to information about your participation in this study.

What information will be collected and used for this study?
If you agree to be in this study, we will collect health information that identifies you. We may collect the results of tests, questionnaires and interviews. We may also collect information from your medical record. We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization. If you do not want to provide authorization, then you cannot participate in this research study.

Who else will see your information?
Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside Northwell Health, except as detailed below.

Investigators will share information collected from this research study with:

- study sponsor and/or its agents,
- other researchers,
- accrediting agencies,
- data safety monitoring board,
- clinical staff not involved in the study who may be involved in participant's treatment,
- health insurers or payers

The following reviewers may access your study and medical records to make sure that this study is being done properly:

- Representatives from federal and state government oversight agencies such as
- Representatives from Medtronic
- Representatives from Northwell Health's Human Research Protection Program (the group of people that oversee research at this institution)

We will do our best to protect the privacy of your records but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by the federal law.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?
If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your treatment, and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records. To request this information, please call the Human Research Protection Program at 516-465-1910.

How long will your health information be kept?
There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. We will keep it as long as it is useful, unless you decide you no longer want to take part or we close the study. You are allowing access to this information indefinitely.

Can you change your mind?

If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the following address:

Albert Fenoy, MD
805 Northern Blvd
Suite 100
Great Neck, New York 11021

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it

Will information about this study be available to the public?
A description of this clinical trial will be available on http://www.Clinical Trials.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 website at any time.

Will my information be used for research in the future?
Information or specimens [collected from you] for this research may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, there will not be an additional consent for future research. By consenting to participate in this study you are agreeing to allow your de-identified specimens and/or data to be used by future researchers without additional consent

Does the investigator of this study receive money if you take part?
The investigators on this study do not receive money for your participation in this study.

Who can answer your questions about this study?
If you have any questions about the study, you may call Dr. Albert Fenoy at (516) 550-2100 or Dr. Miklos Argyelan at (718) 470-8175. If you have questions about side effects or injury caused by research you should call Dr. Albert Fenoy. If you need emergency care, dial 911 or go to the nearest Emergency Room. If you have questions about your rights as a research participant, or concerns about being in the study, or would like to offer input, you may contact the Office of the Institutional Review Board (the committee that oversees research at this institution) at (516) 465-1910. A signed copy of this consent form will be given to you.

[Signature Page Follows]

Summation/Signature

You have read the above description of the research study. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

_____
Printed **Preferred** Name of Participant

_____
Printed **Legal** Name of Participant

_____ _____
Signature of **Legal** Name of Participant Date

_____ _____ _____
Witness's Printed Name Witness's Signature Date
(Note: A witness can be a member of the research team, but cannot be the same person signing consent as the investigator)

Investigator's Statement
In addition to advising the above participant of other forms of treatment and therapy which are appropriate, I have offered an opportunity for further explanation of the risks and discomforts which are/or may be associated with this study and to answer any further questions relating to it.

_____ _____ _____
Investigator's Printed Name Investigator's Signature Date