UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study (this "Research Study")?

Wearable sensor driven closed-loop deep brain stimulation

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Principal Investigator: Aysegul Gunduz, PhD (352) 273-6877

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

Contact information for emergencies after hours or on weekends or holidays: (352) 265-8408 and ask for the neurologist on-call

4. Who is paying for this Research Study?

The sponsors of this study are the University of Florida Department of Biomedical Engineering, Medtronic, LLC, and NIH National Institute of Neurological Disorders and Stroke.

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

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in

this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

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

The purpose of this research study is to evaluate the effectiveness and safety of a possible new treatment for Essential Tremor (ET) using external wearable sensors. It is a therapy called Responsive Deep Brain Stimulation (R-DBS). The study will investigate detection of tremor in ET using wireless external sensors. These sensors will capture muscle activity and the acceleration of your hand (change in speed of your hand). The data from these sensors will be sent to a computer. The R-DBS system will communicate with a computer and apply stimulation when the computer detects tremor. With the detection of tremor, the R-DBS device will initiate a stimulation pattern to suppress tremor activity and improve or alleviate your tremor.

DBS is currently approved for the treatment of ET by the FDA. However, it is approved for continuous stimulation only, so stimulation is delivered even if you are not suffering from symptoms. Continuous DBS stimulation can lead to undesirable side effects such as stuttering and gait/balance problems. We will therefore investigate the effectiveness of R-DBS, which turns on only in response to activity from the sensors; and therefore, will not be on all of the time. Our hypothesis is that R-DBS will provide the same benefit with less side effects. R-DBS will also prolong the battery life of your implant.

There has been evidence that continuous DBS can cause speech changes. To quantify if R-DBS lessens these speech side effects of continuous DBS, we will perform a speech assessment during only one postoperative visit.

For this study, we will be using the Medtronic Nexus-D system, which can communicate with your DBS system. It is an external, battery powered wand, which can also communicate with a laptop computer. Currently, the Nexus-D is used for investigational purposes only.

You are being asked to be in this research study because you have a severe case of ET that has not responded to numerous standard treatments, and you have consented to undergo deep brain stimulation (DBS) surgery within the ventral intermediate nucleus of the thalamus (Vim). Note, that bilateral stimulation of the Vim is investigational. Your participation will be 8 months from the time you provide consent, but overall, there will be 6 post-operative visits within the research study that you will attend. Optional visits after the initial 8 months will be up to you. If you are *only* participating in the speech assessment, there will only be one post-operative visit. However, you have the option to participate in a second research visit after your speech assessment if you would like.

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.

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

We will conduct the following assessments in OFF, ON, and closed-loop stimulation states:

- We will conduct a tremor assessment in which you will be asked to wear wireless sensors that capture muscle activity (also called an EMG) and acceleration information (how fast you move your hand). You will perform various tasks where you will be asked to reach for an object when a red light gives you the cue. We will also ask you to walk with the sensors. We will use data from these sensors to measure the severity of your tremor. We will communicate with the implanted DBS device in your chest cavity with an extension wand and an IPad tablet. We will set your device programming with a Medtronic programmer.
- We will use the Fahn, Tolosa, Marin Tremor Rating Scale (TRS) to assess the severity of your tremor.
- We will use the Quality of Life in Essential Tremor (QUEST) to assess the quality of your life in relation to your essential tremor.

c) What are the likely risks or discomforts to you? Intermittent stimulation may cause tolerance issues or lead to more side effects. Other possible discomforts include common programming side effects such as feeling of tightness, sensory issues such as numbness, tingling, or double vision.

d) What are the likely benefits to you or to others from the research? You could experience improvement in your tremor during your participation in this study. If responsive stimulation is effective and safe, it may be an option for future patients with ET, which would increase the battery life and reduce side effects.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you? Your normal standard clinical care that would be provided for anyone who underwent a deep brain stimulation procedure.

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

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

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

You will continue to receive medical care as you would as a patient diagnosed with essential tremor and scheduled for DBS surgery, or have already undergone DBS.

You will undergo mood, motor and quality of life scales and assessments, as per standard of care, to ensure you are a good candidate for surgery.

After your surgery, you will return to the Fixel Center for Neurological Diseases for standard of care follow up and programming of your device.

7. What will be done only because you are in this Research Study?

If you decide to participate, you will be asked to read, sign, and date this informed consent before any study-related procedures are performed. You will be given the opportunity to ask questions and review the consent before you make a decision.

The following information will be collected from your medical chart and stored for this research study:

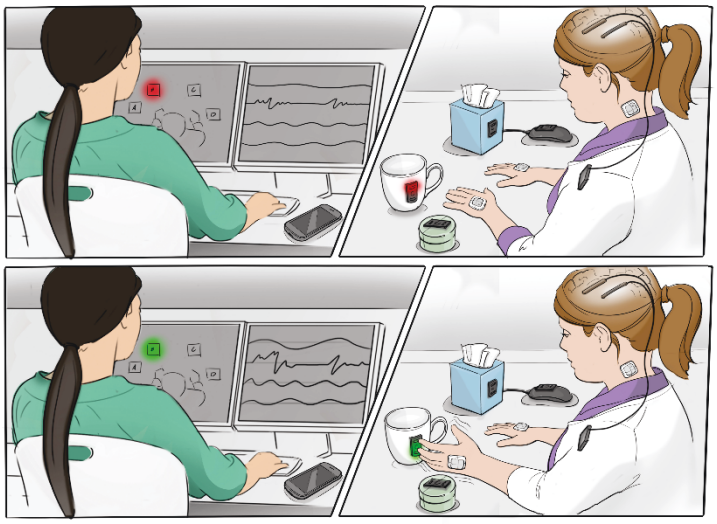
- Name, age, gender, race
- Past medical history
- Medication history
- Substance abuse and alcohol history
- Neurological scans and test results
- Neurological assessments and test results
- Programming visit dates

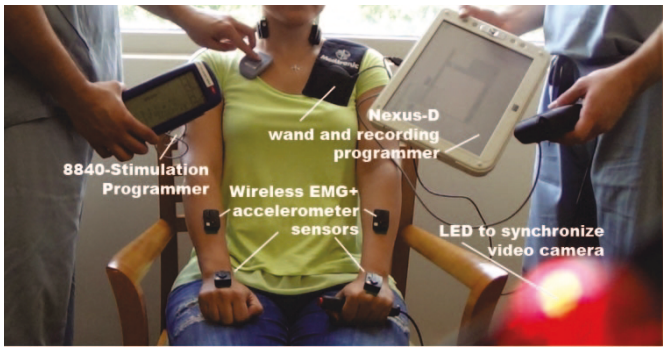
We are obtaining past medical history that concerns any neurological procedures or incidents (i.e. previous neurosurgeries, DBS implantations, or strokes) as these may affect the data we are collecting. We are also collecting data such as previous disease events, time since diagnosis, age at disease onset, etc. Additionally, we are collecting information about substance abuse and alcohol history since substances (i.e. alcohol) affect your tremor, which can ultimately affect the data we are collecting.

Optional Baseline\Preoperative Visit: You will be asked the day before your scheduled surgery to perform some of the tasks outlined below unless you have already undergone DBS surgery. This portion of the research visit should take no more than an hour. This visit will take place in the Neurosurgery Clinic in UF Health Neuromedicine Hospital, East Tower pre-op, or Biomedical Sciences Building.

Postoperative Research Visit: You will return to the clinic for routine programming visits once a month for 6 months. For research purposes only, we will ask you to stay longer after your regularly scheduled programming visit. This portion of the research visit could take up to 6 hours. The visit will take place in the Biomedical Science Building and we will provide transport from the Fixel Center for Neurological Diseases clinic to the Biomedical Science Building. We will record your clinical stimulation settings, and these will be used to program the investigational settings. If you have already undergone DBS and are not scheduled for programming visits since you are optimized, we will ask you to come to the Biomedical Sciences Building for every month for 6 months for research recordings. If you are already enrolled within the study and are undergoing another DBS surgery for your contralateral limb, these visits will again take place after your regularly scheduled programming visit. Instead of 6 monthly visits, you will now perform 12 research visits altogether. We will begin the closed-loop stimulation patterns and begin the following assessments (these assessments will be done in the OFF and ON stimulation states):

- We will conduct a tremor assessment in which you will be asked to wear wireless sensors that capture muscle activity (also called an EMG) and acceleration information (how fast you move your hand). You will perform various tasks where you will be asked to reach for an object when a red light gives you the cue. We will also ask you to walk with the sensors. We will use data from these sensors to measure the severity of your tremor. We will communicate with the implanted DBS device in your chest cavity with an extension wand and an IPad tablet. We will set your device programming with a Medtronic programmer. Please see figures below.





- We will use the Fahn, Tolosa, Marin Tremor Rating Scale (TRS) to assess the severity of your tremor (all post-operative visits).
- We will use the Quality of Life in Essential Tremor (QUEST) to assess the quality of your life in relation to your essential tremor.
- We will audio record your speech during R-DBS, continuous DBS, intermittent DBS, and no stimulation while you produce certain vowel sounds and repeat sentences (one post-operative visits).

This entire visit will be videotaped for a blinded reviewer to review the effectiveness of the new treatment by rating the severity of your tremor. It is a requirement of the study to be videotaped. We will store this video on a secure network only accessible to research personnel associated with this study. After the study is over, the video will be destroyed. Further details on the use of the video are at the end of this consent.

Once the research session is over, your device will be programmed back to your optimal clinical settings.

Single Day Postoperative Research Visit: If you choose to only participate in a single research visit, you will still undergo all the steps listed within Postoperative Research Visit section; however, instead of six monthly visits, you will only participate in one.

Single Day Postoperative Speech Research Visit: If you choose to only participate in a single research visit to assess speech, you will only undergo a speech assessment outlined within the Postoperative Research Visit section. After your speech assessment visit, you have the option to participate in a *second* day of research that will involve the activities outlined in the Postoperative Research Visit section other than the speech assessment.

Optional Postoperative Research Visit: If you have already completed the required 6 months of research visits, for research purposes only, we will ask you to come back even when you do not have a regularly scheduled programming visit. This portion of the research visit could take up to 6 hours. The visit will take place in the Biomedical Science Building. We will record your clinical stimulation settings, and these will be used to program the investigational settings. We will begin the closed-loop stimulation patterns and follow the same procedure as outlined above in the post-operative research visit section. You would not be compensated for these visits if you choose to participate.

This entire visit will be videotaped for a blinded reviewer to review the effectiveness of the new treatment by rating the severity of your tremor. It is a requirement of the study to be videotaped. We will store this video on a secure network only accessible to research personnel associated with this study. After the study is over, the video will be destroyed. Further details on the use of the video are at the end of this consent.

Once the optional research session is over, your device will be programmed back to your optimal clinical settings.

To help us protect your privacy, we have requested a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You have been informed that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. That is, if you give written consent for the release of information, we cannot withhold that information and we cannot hold responsibility for how that person may use your information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. If we learn about child abuse, elder abuse, or intent to harm yourself or others, we will report that information to appropriate authorities.

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

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

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect

- Name, age, gender, race
- Past medical history
- Medication history
- Substance abuse and alcohol history
- Neurological scans and test results
- Neurological assessments and test results
- Programming visit dates

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor (listed in Question 4 of this form);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections.
- Government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state, and local health departments.
- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

We expect your participation will last 8 months from the time you provide consent, but overall, there will be 6 post-operative visits within the research study that you will attend. Optional visits after the initial 8 months will be up to you.

If you opt in for a single visit, your participation will last one day within this study. If you want to participate in the optional second research visit after your speech assessment, your participation will be two days.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

We expect to enroll 20 individuals into the six-month R-DBS study. We plan to enroll 10 individuals to assess speech side effects, but we will sample from the 20 individuals in the six-month R-DBS study. Thus, there will be a maximum of 30 individuals recruited.

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

12. What are the possible discomforts and risks from taking part in this Research Study?

Intermittent stimulation, or responsive stimulation, may cause tolerance issues or might lead to more side effects. We will therefore establish the optimal stimulation patterns to ensure that intermittent stimulation is tolerable. Possible discomforts could occur as a result of taking part in this study from the different stimulation patterns. These possible discomforts could be similar to common programming side effects such as under stimulation, feeling of tightness, sensory issues such as numbness, tingling, or double vision. These can also occur as part of your regular visit. The side effects are stimulation-induced, transitory and pass quickly, since they can be stopped immediately by either turning the device to a lower setting, turning the device off, or returning the device to the normal setting that you use at home.

We will restore your previous therapy settings using a programmer. You will continue to use the settings that were set on your device as part of regular clinic care after the study procedures are complete.

You will perform gait activities which may cause exhaustion. The personnel of the study are highly trained in working with Essential Tremor patients and will remain physically close to you at all times to prevent any fall-related injuries.

There is also the possibility of minor skin irritation at the site where the sensors are placed.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You have been informed that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. That is, if you give written consent for the release of information, we cannot withhold that information and we cannot hold responsibility for how that person may use your information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. If we learn about child abuse, elder abuse, or intent to harm yourself or others, we will report that information to appropriate authorities.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 8-9 in this form discuss what information about you will be collected, used, protected, and shared.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

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

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

There are potential benefits of participating in this study. You could experience improvement in your tremor during your participation in this study. No long-term symptom relief or battery life benefits should be expected from participating in this study. You may experience improvement in your symptoms with the R-DBS settings but at the end of the study, your clinical settings will be put back.

13b. How could others possibly benefit from this Research Study?

If responsive stimulation (R-DBS) is effective and safe, it may provide an option for future patients with ET, which would increase the battery life and reduce side effects.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a scientist. Therefore, the Drs. Gunduz and Okun may benefit if the results of this study are presented at scientific meetings or in scientific journals.

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

You do not have to participate in this study. You will continue to receive care for your ET and regularly scheduled DBS programming.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- If you do not adhere to the required protocol study visits and requirements, you may be withdrawn from the study.
- If the study doctor feels it is in your best interest to be withdrawn from the study.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

Study Services

The Sponsor will pay for or provide the study services/activities required as part of your participation in this study as described above in the question *"What Will Be Done Only Because You Are In This Research Study*". If you receive a bill for these services, please contact Dr. Gunduz at (352) 273-6877.

Items/Services Not Paid for by the Sponsor

Any other medical services provided to you that are not directly required by this study will be billed to you or your insurance company in the usual manner. Note we are not paying for your DBS surgery. We are approaching you for research that will take place only after the surgery.

17. Will you be paid for taking part in this Research Study?

You will be compensated $25 for each post-operative research assessment, excluding the optional visits. Study visits for which you might stay overnight to ease the burden of travel, hotel accommodations will be provided and arranged for you by study staff.

18. What if you are injured while in this Research Study?

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

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or

research-related injuries. Please contact your insurance company for additional information.

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

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the Research Team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this Research Study.

SIGNATURES

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

Signature of Person Obtaining Consent and Authorization _____ Date _____

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

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

Signature of Person Consenting and Authorizing _____ Date _____

Consent to be Video and Audio Recorded

Your name or personal information will not be identified on the video recordings, and confidentiality will be strictly maintained. However, when this video recording is shown or heard, others may be able to identify you.

The Principal Investigator (PI) of this study, Dr. Aysegul Gunduz, or her successor, will keep the video recording in a locked cabinet, in a folder on a password protected computer server drive, or as an encrypted electronic file. This video recording will be shown under his direction to students, researchers, doctors, or other professionals and persons.

Please indicate under what conditions Dr. Gunduz has your permission to use the video recording, and initial below.

☐ The following will be **destroyed once the study is closed (required for participation)** (initial):

_____ video recording(s)

_____audio recording(s)

☐ For the purposes of **education at the University of Florida Health Science Center**. The PI may keep the video and audio recording for up to 6 years after the study is over, in a locked file, in a password protected computer server drive, or as an encrypted electronic file (initial next to all that apply):

_____ yes _____ no

☐ For the purposes of **education at the University of Florida Health Science Center; and for presentations at scientific meetings outside the University**. The PI may keep the video and audio recording for up to 6 years after the study is over, in a locked file, in a password protected computer server drive, or as an encrypted electronic file:

_____ yes _____ no

_____ _____

Signature Date