FDA PRINCIPAL INVESTIGATOR: Daniel X. Hammer, PhD

NIH CO-PRINCIPAL INVESTIGATOR: Catherine Cukras, MD, PhD

STUDY TITLE: Adaptive Optics Imaging of Outer Retinal Diseases

STUDY SITES: Optical Diagnostic Devices Laboratory
U.S. Food and Drug Administration (FDA)
10903 New Hampshire Ave
Building 62, Room 1106
Silver Spring, MD 20993

National Institutes of Health (NIH)
NIH Clinical Center (CC)
10 Center Drive
Bethesda, MD 20810

NIH IRB NUMBER: 000187

Cohort: Standard

Consent Version: 4/26/2021

Key Information about this Research

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH) and the Food and Drug Administration (FDA). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH and FDA is your choice. Please ask the research staff to explain any part of this form that is not clear to you. Before you decide if you would like to volunteer you should completely understand the possible risks and benefits of the study.

After reading this consent form, having the study fully explained to you, and having all your questions answered, if you agree to participate in the study, you will be asked to sign this form.

This research study will assess a new type of high resolution retinal imaging technology that uses adaptive optics (AO). AO senses the way your eye distorts light and corrects imaging beams to allow very sharp pictures of the back of your eye (the retina) to be taken. The retina is the back part of your eye that senses light and sends images to your brain, which helps you do activities like reading, driving, and seeing small details. Retinal diseases can affect your vision and be serious enough to cause blindness.

For this study, we use the term 'eye exam' to mean the initial screening exam at the NIH eye clinic and 'imaging session' to mean imaging on the investigational AO retinal imager at FDA. Both the NIH eye exam and the FDA imaging session will take approximately two to three hours (not including recovery from dilation). Generally, we will dilate and image only one eye for the imaging sessions (the same eye each time) but both eyes will be dilated and checked at the eye exam. Before we start, we will notify you if, for your session, we need to image both eyes (the total estimated time of two to three hours will not change if we image both eyes). For both the NIH eye exam and the FDA imaging session, eye dilation drops will be used to dilate your eyes. Photophobia (sensitivity to light) from enlarged pupils will occur after both the eye exam and imaging session, and you will be given disposable sunglasses to wear until the dilating drops wear off (around four to six hours after administration). Until the eye drops wear off, you should not drive or participate in any other activity where vision is needed to avoid hazards. If you plan to drive to and from the screening exam and imaging sessions, you may want to come with someone who can provide transportation.

This technology may eventually be used to help diagnose and guide treatment of eye diseases. The AO imaging device used in this study is an investigational device, which means that it has not received FDA approval.

Purpose of this Study

The purpose of this study is to evaluate new high magnification imaging technology called adaptive optics which includes new hardware, processing and analysis software algorithms, and methodology that may be helpful to detect and guide treatment of eye disease.

Test Protocol and Duration

The study will take place at the NIH National Eye Institute (NEI) (Clinical Center, Building 10, Ophthalmology Clinic, Floors 10-11) and at the FDA White Oak Campus (Building 62, Room G238). See accompanying maps for directions and security checkpoint instructions. We expect to enroll up to a total of up to 100 participants, including up to 50 participants who have been

diagnosed with outer retinal diseases or conditions (e.g., age-related macular degeneration, cone-rod dystrophies, hydroxychloroquine toxicity, retinitis pigmentosa, etc.) and up to 50 healthy volunteers. Depending on the experiment, you may be asked to attend imaging sessions over three years. The sessions can be scheduled to occur anytime that meets your schedule. The minimum time between imaging sessions at the FDA will be one week and the maximum number of imaging sessions in one year will be five. The maximum number of eye exams at the NIH will be three per year over three years.

At least one week prior to the first imaging session at FDA, you will receive a full eye exam by an ophthalmologist at the NEI who will also assess any risks associated with dilating drops.

NIH Eye Exam

We will review your medical records and confirm your participation in an NEI study. We will use this information and examine other eligibility criteria to determine whether you can participate in this study.

You will have some or all of the following examinations and tests at each study visit to the NIH. An eye dilation and AO imaging session will be performed at every visit to the FDA. AO imaging will be completed at the FDA only:

- Eye Examination, Dilation and Photography: The eye examination includes testing how well you see, measuring your eye pressure, and looking at the front of the eye to evaluate safety of dilation. To examine the inside of your eye, we will use eye dilation drops. While your eyes are dilated, we will measure the thickness of your retina and observe your eyes for 30 minutes to make sure you do not have a reaction to the eye drops. We will also take pictures of the retina and the inside of your eyes.
- Biometry: We will take measurements of your cornea (the clear, front part of your eye) and the length of your eye.
- Perimetry: We may test how well you can detect different levels of light. You will be seated in front of a computer screen and asked to press a button when you see a light on the screen.

After the eye exam, an ophthalmologist will assess the ocular risk of further participation as you may be excluded if the risk of reaction to the eye drops, as determined by the ophthalmologist, is high. You may also be excluded from further participation if you meet the exclusion criteria, which includes predisposition to (i.e., narrow iridocorneal angle) or any history of acute angle closure glaucoma (AACG), visual correction outside the range +4 diopters (D) to -8 D, or eye pathology that prevents adequate imaging.

FDA Imaging Session

Once you have been screened and cleared by the ophthalmologist to continue participation in the study, we will schedule you for an imaging session at the FDA. During each imaging session, you will be given eye dilation drops by trained research staff to dilate your pupil(s). The eye drops are necessary to collect optimal images, and if you are uncomfortable receiving them or know of any history of reaction, you should not participate in the study. Staff will monitor your eyes in general during the entire imaging session for any adverse events.

After your pupils dilate, you will be asked to sit and place your chin on a rest to stabilize your head and look into the imaging instrument. While looking into the instrument, you will observe several lights. The investigator will describe what you will see and give you instructions on what to look at. The investigator may also ask you to periodically blink. Beams of light will be directed to your eyes to take images of your retina. At no point will anything touch your eye. You will be given rest periods after scans to avoid fatigue where you will be asked to sit back from the instrument. You may ask for additional rest periods at any time during the experiment. During the imaging sessions, video sequences of different regions of your retina will be collected.

Potential Risks and Discomforts

Participating in research may result in an injury. If you suffer an injury directly related to your participation in this study, the study researchers will help you obtain medical treatment for the specified injury. If for any reason you notice changes in your vision after the eye exam or imaging session, contact the PI and if you feel the severity of the changes to your vision are significant, you can request and will receive an additional eye exam by Dr. Cukras or another ophthalmologist at the NIH at no cost to you.

The potential risk of injury from participation in the study include: (1) risk of reaction to the dilating eye drops (an increase in internal eye pressure), (2) risk of exposure to light levels that can lead to eye injury, and (3) risk of injury from exposure to laboratory instruments. This study may also involve risks that are currently unforeseeable.

The eye drops are commonly used by optometrists and ophthalmologists. You may feel a brief burning or stinging sensation when the drops are first placed in your eyes; this is normal. If you know of any history of reaction to pupil dilating drops, you should not participate. You will also notice a higher sensitivity to light after the exam, and you should avoid outdoors and bright lights. Sunglasses will be provided for use until the drug wears off (typically within four to six hours of administration). Other adverse reactions (from the drug label information) include dryness of the mouth, tachycardia, headache, allergic reactions, nausea, vomiting, pallor, central nervous system disturbances and muscle rigidity. If any urgent medical issues arise during your imaging session at the FDA, the FDA investigator will call 911.

All light levels from the imaging beams are accurately measured each day before any participants are imaged and are below maximum safe power level established by the American National Standards Institute (ANSI standard Z 136.1 – 2014). The AO imaging device also includes several components and functions that prevent unsafe light levels from entering your eye.

Possible Benefits of and Alternatives to Participation

There is no direct benefit of participation to you. You will receive no treatment. However, results from the study may help improve high resolution AO retinal imaging technology, and how it is evaluated by the FDA, which may provide a benefit to future patients with eye disease (including outer retinal diseases). Your clinical care will not be affected in any way if you choose not to participate or withdraw from the study. There are no alternatives to participation, beyond choosing not to participate.

Data Storage and Use

Your participation and all records obtained from this study will remain confidential to the extent permitted by law. For the initial NIH eye exam, records will be kept at the eye clinic in the same manner as records from participants in other NIH-sponsored clinical studies. Information will be stored in the NIH's Electronic Medical Record (EMR) system, which is accessible only by trained staff on password protected computers. All participant information remains on-site at the NIH/NEI and is accessible only by trained staff and maintained with confidentiality abiding by NIH policies and all relevant regulations regarding medical records. Your clinical data from the eye exam will be transferred to the FDA investigators so that we may properly interpret the AO images. All transferred clinical data will be labeled with a code and will not contain your name or other information directly identifying you. Except where stated below, access to the clinical data is limited to the study researchers listed above and to those who receive authorization for access from the research team, sponsor, and/or agents of the sponsor.

For the FDA imaging session, the only identifying information we will collect is your name, age, and sex, and we will keep this information confidential to the extent permitted by law. Your name, age, and sex will not be stored with your images or data. Images obtained from the imaging session will be stored at the FDA on password protected computers that are accessible by trained staff only and maintained with confidentiality abiding by the FDA policies.

The images and data will be used publicly for research and educational purposes, including in publications and presentations, and may be viewed by internal and external professional colleagues, students, and other trainees. When we disclose information about this research to the public, we will take steps to ensure that the images or data disclosed cannot be linked back to you so that confidentiality will be maintained: Personally identifiable information (PII) will be

removed from all NIH clinical data in a process called de-identification, and FDA AO images and data contain no PII. The de-identified images and data may be shared with our research team, including external collaborators, as well as the sponsor and their agents.

Risks of Data Storage and Sharing Data

When we store your data, we take precautions to protect your information from others that should not have access to it. When we share your data, we will do everything we can to protect your identity, for example, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your data.

Saving Data for Use in Other Research Studies

In addition to the use and sharing of your retinal images and data described above, we will remove any information from your images and data that can identify you such as name, address, or medical record number, and then use the images and data for additional research studies at the NIH, FDA, or other places. If we do this, we will not contact you to ask your permission or otherwise inform you. By signing this document, you consent to sharing de-identified study data.

Your images and data may be shared with others, including those not at NIH and FDA. Your images and data may be sent to a repository for storage. Your images and data may be used for other research projects, including those not related to your condition if you agree. Some repositories restrict access to the images and data they contain to researchers and projects they approve. Some repositories permit unrestricted access.

Research using images and data from this study may lead to new tests, drugs, or devices with commercial value. You will not receive any payment for any product developed from research using your images and data.

If you are enrolled in other studies at NIH, your data and images may be shared with investigators of those studies. The data and images may be shared with your name and identifying information. Sharing these data and images will help minimize your need to repeat procedures if data or images are already collected.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. These researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether

your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

Sharing Clinical and Other Test Results With Participants

We will give you the results of all of your clinical examinations. We will not provide information about your health to others, including family members. With your written request, we will send reports to your own doctors

Sharing the Results of the Research Study With Participants

We will share with you any information we learn that may relate to your willingness to continue to participate in the study. If you would like, we will share with you any published scientific papers from this study. Please keep us updated with your address if you would like to receive this information.

Clinical Trial Registration and Results Reporting

A description of this clinical trial will be available on https://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Participation and Withdrawal

Your participation in this research is completely voluntary. You may choose not to take part at all. If you decided to participate in this research, you may withdraw from the study at any time by notifying the PI. If you decide not to participate in this study or end participation, you will not be penalized or lose any benefits to which you otherwise qualify. If you are an NIH patient and decide not to participate or end participation, your NIH medical care will not be affected. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. The investigators may also end your participation in this study if he or she feels that your participation presents any safety concern. You will be informed if any significant new findings are discovered that may affect your willingness to participate in the study.

Compensation, Reimbursement, and Payment

Will I receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will receive a $25 gift card at the end of each FDA visit as compensation for small travel expenses. Parking at the FDA campus visitor lot is free.

Will I receive reimbursement or direct payment by NIH as part of my participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

You will be given stamps as reimbursement from the NIH to park without cost on the NIH campus. There are no other costs associated with your participation in this study.

If you are unable to finish the study, you will be able to keep the gift cards for the parts you completed. You will no longer continue to receive compensation if you are unable to complete the study.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will taking part in this research study cost me anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center. There is no additional cost related to the FDA AO imaging session.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the FDA, which are involved in keeping research safe for people.
- The Institutional Review Board that is reviewing the research to ensure the rights and welfare of participants are protected.

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of data, and as further outlined in the following sections.

Certificate of Confidentiality

To help us protect your privacy, this research is covered by a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH and FDA researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.
The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH or the FDA; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research. The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is

involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

Conflict of Interest (COI)

The National Institutes of Health (NIH) reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

No NIH or FDA investigator involved in this study receives payments or other benefits from any company whose drug, product or device is being tested.

NIH Policy Regarding Research-Related Injuries

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

Rights as a Research Subject and Contact Information for Problems or Questions

If you have any questions about your participation in the study you may call or email the Principal Investigator, Daniel X. Hammer, PhD, at 301-796-9320 or daniel.hammer@fda.hhs.gov. If you have questions about any aspect of your medical care related to study participation, contact the Co-Principal Investigator, Catherine Cukras, MD, PhD, at NIH/NEI, 301-435-5061 or cukrasc@nei.nih.gov. You may also contact Daniel Claus at the NIH/NEI at 301-451-1621 or Daniel.claus@nih.gov. In the case of a medical emergency, call 911. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

The Food and Drug Administration Institutional Review Board (IRB) oversees all FDA human subject studies and ensures that the rights of research participants are protected. The FDA IRB has reviewed this research study and may review the records of your participation in this research to ensure that proper procedures are followed.

If you have questions about your rights as a study participant or concerns about how you are treated in the study, you may contact FDA Human Subject Protection Program at 301-796-9605 or HSPPMS@fda.hhs.gov.

You have not waived any legal right to which you are legally entitled by signing this form.

Consent Statement

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Subject # _____