H-44616- THE EFFECTIVENESS OF HIGH RESOLUTION MICROENDOSCOPY (HRME) IN HIGH GRADE INTRAEPITHELIAL LESIONS (HSIL) DIAGNOSIS FOR PEOPLE LIVING WITH HIV

Background

You are invited to take part in a research study. Please read this information and feel free to ask any questions before you agree to take part in the study. We are testing a new instrument or "camera probe" to see if we can get better pictures of abnormal areas of the anal canal in people at risk of anal high grade intraepithelial lesions (HSIL) or anal pre-cancer in order to make an HSIL diagnosis without the need for a biopsy. The standard of care procedure is a type of anoscopy procedure (procedure to examine a person's anal canal) using Lugol's Iodine as a dye or stain for abnormal areas or areas that might be diseased. This procedure often requires a biopsy to make the diagnosis of anal pre-cancer.

You are scheduled or going to be scheduled for this procedure by your doctor for your regular medical care. We are comparing the 2 kinds of imaging, so all subjects will get the standard AND the new type of imaging with the probe.

A researcher at Rice University in Houston, Texas, who is collaborating or sharing knowledge on this study, holds patents (ownership rights given by law) to the specimen imaging probe being used. The technologies have been licensed to Remicalm LLC in which the Rice University researcher holds an ownership stake.

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.

This research study is funded by National Cancer Institute

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Purpose

The purpose of this study is to find out if the use of a medical imaging instrument called a mobile high resolution microendoscope (mHRME) can help doctors see abnormal tissue in subjects with anal high grade squamous intraepithelial lesion (HSIL) also called anal pre-cancer without having to conduct biopsies, or take a piece of tissue. Squamous cell cancer of the anus (SSCA) is one of the most common cancers among HIV-infected individuals in the United States.

Current HIV primary care guidelines recommend yearly anal screening for pre-cancer, but the screening has some disadvantages including cost, availability, number of visits, and patient discomfort. Our group has developed the mHRME (mobile high resolution microendoscope) that allows doctors to see changes at the cellular level on the anal canal tissue using the camera probe, without needing to take biopsies, or pieces of tissue. This will allow doctors to make a pre-cancer diagnosis using only pictures from the mHRME rather than taking biopsies or pieces of tissue from the patient, and sending the tissue for review by a pathologist, simplifying and decreasing the cost of the procedure.

The specimen imaging probe (mHRME) being used in this study is considered investigational or being

research because it has not been approved by the Food and Drug Administration (FDA). Because the probe is experimental no formal instructions for cleaning the probe exist; therefore our procedure for disinfecting and sterilizing the probe is based on instructions for a similar, commercially available probe made from identical materials. The use of the probe also requires Proflavine, a contrast agent (dye) which was developed as an antibacterial agent, to be sprayed on the tissue in the anal canal to highlight abnormal areas. The use of this contrast agent is also considered investigational because it is not approved by the Food and Drug Administration (FDA) for this use. We are testing this new probe and Proflavine against the standard way of finding SCCA which is Lugol's dye and the usual anoscope to see how well a picture-based diagnosis is compared to the diagnosis identified by biopsy.

Procedures
A total of 200 subjects at 2 institutions will be asked to participate in this study.
You will be one of approximately 75 subjects to be asked to participate at this location.

In order for the researchers to get enough information on the imaging devices, a large number of patients need to be enrolled in the study.

The research will be conducted at the following location(s):
Baylor College of Medicine, HCHD: Thomas Street Clinic, and Mount Sinai School of Medicine - New York.

Study Participation (will be one time in-person participation)

If you are not one of the first 50 subjects enrolled in this study, you will be asked to answer a few questionnaires. If you do not want to complete the questionnaires, you do not have to.

The questionnaires include: a behavioral questionnaire that includes Demographics (age, race, gender, etc.), use of tobacco, alcohol and drugs or illicit substances; history of genital condyloma (warts); frequency of condom use; sexual behavior, date of HIV diagnosis; history of sexual transmitted diseases or opportunistic infections; previous history and treatment of HPV-related anogenital disease; including history of anal cytology or HRA; use of hormonal agents or medications; and HIV cART regimen and self-reported adherence; a questionnaire that measures the quality of life called EQ-5D that asks questions on the degree of mobility, self-care, usual activities, pain/discomfort and anxiety/depression you might have.

We will review your medical records for the most recent viral load, CD4 count, and anal cytology or biopsies.

We will do an outer inspection of your anal and genital areas to record the presence and size of condyloma or genital warts, as well as the presence of other genital lesions on all subjects, and a digital

rectal exam will be performed on all patients. The digital rectal exam is a simple procedure where the doctor will insert his/her index finger into the anus to check for abnormalities such as hemorrhoids, lumps or rashes.

A (polyester) Q-tip premoistened with water will be used to obtain cells and HPV DNA and information about the squamous cells from the anal canal. Standard of Care high-resolution anoscopy (HRA) will also be performed on the initial visit to provide a visually-directed anal biopsy (or collection of pieces of tissue). Areas suspicious for HSIL or pre-cance in the anal epithelium as identified by the physician will be sampled with cervical biopsy forceps. If there are no suspicious lesions seen on HRA, a random biopsy, preferably in the left lateral quadrant, will be performed. These biopsies may be performed during regular, standard of care HRAs, so they are not specific to research.

The mHRME images will be obtained from all areas identified as abnormal by the physician and from one normal area. The mHRME procedure as well as standard HRA and biopsy time will be recorded. In addition, your biopsies (pieces of tissue) will be sent to at least one other pathologist to make sure that the diagnosis is correct.

All patients will be contacted at 48 hours and at 1 month by a coordinator to determine if there are any adverse events recorded in both groups (bleeding, infection, and pain). The (EQ-5D) questionnaire will also be given to the patients at each follow-up contact.

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.
What protected health information is collected and used in this study, and might also be disclosed (shared) with others?
As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, telephone/fax numbers, DOB, age, gender, race, social security number, medical records number, health plan numbers, biometric identifiers, photographic images, videotapes, and/ or audiotapes of you.

Additional information for Mount Sinai patients:

The researchers will also get information from your medical record at Mount Sinai Hospital. We will review your medical records for the most recent viral load, CD4 count, and anal cytology or biopsies.

During the study the researchers will gather information by:
- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)

- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- reviewing HIV-related information, which includes any information indicating that you have had an HIV related test, or have HIV infection, HIV related illness or AIDS, or any information which could indicate that you have been potentially exposed to HIV
- reviewing alcohol and/or substance abuse records

Why is your protected health information being used?
Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.
The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.
The research team and other authorized members of The Mount Sinai Health System (Mount Sinai) workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School¿s Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?
As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations:
- Other collaborating research center(s) and their associated research/clinical staff who are working with the investigators on this project: Baylor College of Medicine, Rice University, University of Texas School of Public Health, and University of California San Francisco
- The sponsoring government agency and/or their representative who need to confirm the accuracy of the results submitted to the government or the use of government funds: National Cancer Institute
- Contract Research Organization (whose job is to help organizations fulfill their responsibilities in the research and development process): Baylor College of Medicine and Affiliated Hospitals
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Department of Health and Human Services and the Office of Human Research Protection.

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

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

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

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

Notice Concerning HIV-Related Information

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

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

Research related health information

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you sign this document, you give permission to people who give medical care and ensure quality from Baylor College of Medicine, HCHD: Thomas Street Clinic, and Mount Sinai School of Medicine - New York to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes:

- Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.
- Specific information concerning alcohol abuse
- Specific information concerning drug abuse
- Specific information concerning HIV
- Demographic information (name, D.O.B., age, gender, race, etc.)
- Full Social Security #
- Partial Social Security # (Last four digits)
- Photographs, videotapes, and/or audiotapes of you

The health information listed above may be used by and or disclosed (released) to researchers, their staff and their collaborators on this research project, the Institutional Review Board, Baylor College of Medicine, HCHD: Thomas Street Clinic, Mount Sinai School of Medicine - New York, and NATIONAL INSTITUTES OF HEALTH (NIH) and their representatives.

Agents of the U.S. Food and Drug Administration may inspect the research records including your health information. Agents of regulatory agencies such as the U.S. Department of Health and Human Services will be permitted to inspect the research records including your health information.

The data coordinating center will have access to the research records including your health information.

A Data and Safety Monitoring Board will have access to the research records including your health information.

Use or Disclosure Required by Law

Your health information will be used or disclosed when required by law.

Your health information may be shared with a public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability and conducting public health surveillance, investigations or interventions.

Baylor College of Medicine, HCHD: Thomas Street Clinic, and Mount Sinai School of Medicine - New York are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine, HCHD: Thomas Street Clinic, and Mount Sinai School of Medicine - New York to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

Please note that the research does not involve treatment. Baylor College of Medicine, HCHD: Thomas Street Clinic, and Mount Sinai School of Medicine - New York may not condition (withhold or refuse) treating you on whether you sign this Authorization.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers, their staff and their collaborators on this research project, the Institutional Review Board, NATIONAL INSTITUTES OF HEALTH (NIH) and their representatives, regulatory agencies such as the U.S. Department of Health and Human Services, FDA, Baylor College of Medicine, data coordinating center, Data and Safety Monitoring Board, HCHD: Thomas Street Clinic, and Mount Sinai School of Medicine - New York may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. If you revoke this Authorization, you may no longer be allowed to participate in the research described in this Authorization.

To revoke this Authorization, you must write to: Dr. Elizabeth Chiao Baylor College of Medicine One Baylor Plaza, MS: BCM271 Houston, TX 77030

This authorization does not have an expiration date. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Potential Risks and Discomforts
Many side effects go away soon after the procedure, but in some cases, side effects may be serious, long-lasting or permanent, and may even cause death. It is important that you tell the study staff about any side effects that you may have had even if you do not think it is related to the procedure.

Allergic reaction
There is the possibility of an allergic reaction to the Proflavine contrast dye in which you may have local irritation. The effect should be temporary and antihistamines can be given to treat the irritation.

Specimen Imaging Probe
There are no known risks from the use of the imaging probe.

Anal biopsies
The risks associated with anal biopsies include: pain, bleeding and a small risk of infection. The biopsies are standard of care procedures and would happen whether or not you enrolled in the study.

If you experience any symptoms other than those that your study doctor has informed you are associated with the procedure, please let your study doctor know.

Pregnancy
Insufficient information is available on the use of Proflavine in pregnancy. Drugs can have harmful effects on the fetus at any stage of pregnancy.

Loss of Privacy
There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk. Your name, medical record number, or other information that could identify you will be replaced on research forms with a subject identification number. You will not be identified by name in any study information. We will store anything with your name or other identifiers in locked files. The study team will have your name and other identifiers but will not share that with anyone outside the study team.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

In addition to these risks, this research may hurt you in ways that are not known. The unknown risks might be minor or might be major (death).

There may be unknown risks or discomforts involved. Study staff will update you in a timely way on any new information that may affect your decision to stay in the study. There is a small risk for the loss of confidentiality. However, the study personnel will make every effort to minimize these risks.

Potential Benefits
You will receive no direct benefit from your participation in this study. However, your participation may help the investigators better understand The benefits of the study is that the mHRME probe may be able to detect HSIL without the need for invasive biopsies. There is a possibility for others infected with HIV and HPV in the future to benefit from this research. .

Alternatives
The following alternative procedures or treatments are available if you choose not to participate in this study: You may choose to undergo standard high resolution anoscopy (HRA) without obtaining images using the mHRME probe. .

Subject Costs and Payments

You and/or your insurance company will be responsible for the standard of care costs (high resolution anoscopy and biopsies). There is no cost for participating in this research study.

You will be paid $50.00 for taking part in this study.

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

Research Related Injury

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this medical care will be billed to you and/or your health care insurance. In some cases, the costs of this care may be paid by someone else. In the event of injury, contact the Principal Investigator.

This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

In the event of Injury resulting from this research, Thomas Street Clinic (TSC), Anal Dysplasia clinic at the Mount Sinai Medical Center (Dr. Gaisa) in New York City are not able to offer financial compensation nor to absorb the costs of medical treatment. However, necessary facilities, emergency treatment and professional services will be available to you, just as they are to the general community.

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Women of Childbearing Potential

It is possible that the medicines used in this study could injure a fetus if you or your partner becomes pregnant while taking them. Because of the potential risks involved, you or your partner should not become pregnant while you are participating in this study.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

The investigator, SHARMILA ANANDASABAPATHY, and/or someone he/she appoints in his/her place

will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: ELIZABETH YU CHIAO at 713-794-8666 during the day and Immunocompromised MD Service at Ben Taub General Hospital 713-798-6970 after hours for Thomas Street Clinic patients.

For Mount Sinai patients, please contact site PI Dr. Michael Gaisa at 212-241-3150. Physical address: 17 East 102nd Street, New York, NY 10029. Mailing address: One Gustave L Levy Place Box 1087, NY, NY 10029

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date