Title of Study: Advanced Gastrointestinal Endoscopic Imaging	
Title of Consent (if different from Study Title):	
Principal Investigator: Shai Friedland, MD	VAMC: VA Palo Alto HCS

Are you participating in any other research studies? _____ yes _____ no

INTRODUCTION TO RESEARCH STUDIES

A research study is designed to answer specific questions, sometimes about a drug or device's safety and its effectiveness. Being in a research study is different from being a patient. When you are a patient, you and your personal doctor have a great deal of freedom in making decisions about your health care. When you are a research subject, the Protocol Director and the research staff will follow the rules of the research study (protocol) as closely as possible, without compromising your health.

PURPOSE OF RESEARCH

Your doctor(s) may have referred you to the endoscopy unit today for a routine endoscopy for intestinal cancer screening, or you may be receiving care in the gastroenterology or general surgery department. If you are not undergoing endoscopy today, you are invited to participate in a research study examining whether a new blood test can detect colon cells in the blood. 3 tubes of blood will be collected from your vein. No other research interventions will be performed in this case.

If you are undergoing endoscopy today, in addition to your scheduled endoscopy, you are invited to participate in a research study of advanced endoscopic imaging. This is a clinical study to evaluate whether more detailed (better) images of the gastrointestinal tract can help physicians locate abnormalities (irregularities), such as pre cancer or early cancer of the intestinal tract, more easily. Endoscopes (flexible tubes with camera and light source at the tip) usually produce an image through the use of white light. In advanced endoscopic imaging, the endoscopes create images that are finer, larger or of varying colors through adjustments in the light. They produce an overall more detailed picture of the GI tract, that may in turn, make abnormalities in the GI tract, such as pre-cancer and early cancer, more noticeable. A sleeve (overtube) will also be used to stabilize the tip of the endoscope. A short transparent cap will also be placed at the tip of the endoscope to improve visualization. We will assess whether the cap improves visualization and stability of the endoscope during the procedure. The instruments used in this study are experimental and are not FDA approved. If a polyp is removed during your endoscopy, we may add a small amount of a medication called tranexamic acid to the polyp injection to see if it improves our ability to see the polyp by reducing small amounts of bleeding. To perform polyp removal for very small polyps ($\leq$3mm), we may use cold snare or biopsy forceps to remove your polyp,

to see which technique is better for removing polyps completely. For polyps ≥3mm, we may use a lifting agent (EverLift) to help with removal of the polyp, to see if use of a lifting agent will improve ability to remove polyps completely. The EverLift™ device has been cleared by the FDA as an aid to help lift polyps prior to removal with another device (e.g., snare) but are not cleared for removing the polyps entirely without the use of another device. The use of the EverLift device is considered experimental in this study. Further, if a polyp is removed during your endoscopy, we may perform biopsies at the site of the polyp removal to check for completeness of polyp removal. We are also interested in understanding the impact of COVID-19 on endoscopic findings. During pathological review, we may check for residual COVID-19 DNA in your biopsy sample. You were selected as a possible subject in this study because you are already scheduled to undergo an endoscopy for cancer screening.

Your participation in this study is entirely voluntary.

Your decision whether or not to participate will not prejudice you or your medical care. If you decide to participate, you are **free to withdraw** your consent and to discontinue participation at any time without prejudice to you or effect on your medical care. If you decide to terminate your participation in this study, you should notify Dr Friedland at (650) 493-5000 x 64800.

This research study is looking for 1,100 patients undergoing endoscopy at Stanford University or the Palo Alto VA hospital. 1,000 patients referred for endoscopy to the VA Palo Alto Health Care system will be enrolled in the study.

DURATION OF STUDY INVOLVEMENT

Your participation in this research study is expected to take approximately 10 minutes.

PROCEDURES

If you choose to participate, in addition to the usual light colonoscopy that you are having performed today, Dr. Friedland and his research study staff will also perform an examination of the intestinal tract with an advanced imaging technique and use a computerized image analysis software. In this examination, we will use a mini optical scope that can be placed inside of the clinical endoscope. This mini-scope is much like the other tools we use in the endoscope in that it fits similarly into the endoscope. This mini-scope will be used to create

better pictures, finer images of higher resolution, of the surface of your colon. This will add approximately 10 minutes to the routine procedure time.

In addition, if biopsies are performed during your procedure then a portion of the biopsy material will be analyzed by the researchers using the mini-scope and biomarker assays and then destroyed when the study is complete. A normal biopsy sample may also be taken for comparison purposes, in which imaging with the mini-scope and analysis with biomarker assays may be performed. In addition, 2 or 3 tubes of blood will be collected from your vein. If a polyp is removed during your endoscopy, we may add a small amount of a medication called tranexamic acid to the polyp injection to see if it improves our ability to see the polyp by reducing small amounts of bleeding. To perform polyp removal for very small polyps ($\leq$3mm), we may use cold snare or biopsy forceps to remove the polyps, to see which technique is better for removing polyps completely. For polyps $\geq$3mm, we may use a lifting agent (EverLift) to help with removal of the polyp, to see if the lifting agent improves ability to remove polyps completely. If a polyp is removed during the endoscopy, we may perform biopsies at the site of the polyp removal to check for completeness of polyp removal.

If you currently have or recently had COVID-19, for the biopsies that we perform during your endoscopic procedure, we may plan to check for residual COVID DNA in the biopsies.

SUBJECT'S RESPONSIBILITIES

You should:

- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

While participating in this research study, you should not take part in any other research project without approval from all of the Protocol Directors. This is to protect you from possible injury arising from such things as extra blood drawing, extra x-rays, the possible interaction(s) of research drugs, or other similar hazards.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are **free to withdraw** your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If you would like to withdraw from the study, please tell Dr Friedland or any of the nurses or physicians in the endoscopy unit and you will be immediately withdrawn from the study. In that case you will have your regularly scheduled endoscopy and no advanced imaging endoscopy will be performed.

The Protocol Director may also withdraw you from the study and the study medication may be stopped without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- Pregnancy
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions.

- The advanced imaging endoscopy procedure will add approximately 10 minutes to the procedure time for your scheduled endoscopy
- As in all types of endoscopy, there is a small (less than 1 in 200) risk of bleeding, perforation of the intestine, or respiratory depression from the

sedation. To minimize the risks, we will stop the exam if you experience significant pain.

- The advanced imaging endoscopy procedure may involve currently unforeseeable risks.
- There is a small risk of an allergic reaction or other rare side effect from the Tranexamic acid
- There is a small risk of bleeding (less than 1 in 1,000) and infection (less than 1 in 1,000) in obtaining biopsies at the site of polyp removal.
- There is a very small risk (less than 1 in 5000) of bleeding or perforation from the endscope cap used during the procedure

POTENTIAL BENEFITS

- There is a small possibility that the advanced imaging endoscopy will result in finding a growth or other disorder in the gastrointestinal tract that will benefit you.
- **WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY.**

ALTERNATIVES

The alternative to the study is not to participate, in which case you will simply undergo the endoscopic procedure for which you are already schedule and no advanced imaging endoscopy will be performed.

SUBJECT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction.

If you decide not to participate, tell the Protocol Director. You will still receive care for your disease and will not lose any benefits to which you would otherwise be entitled.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study

CONFIDENTIALITY

Your identity will be kept as confidential as possible as required by law. Except as required by law, you will not be identified by name, social security number, address, or telephone number. Your research records may be disclosed outside of Stanford, but in this case, you will be identified only by a unique code number. Information about the code will be kept in a secure location and access limited to research study personnel.

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. However, your identity will not be disclosed**.**

Patient information may be provided to Federal and other regulatory agencies as required. The purpose of this research study is to obtain data or information on the safety and effectiveness of miniaturized microscopes and dyes that can be used with these microscopes to better identify cancer; the results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required. The dyes have already been approved by the Food and Drug Administration. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

FINANCIAL CONSIDERATIONS

PAYMENT: You will not be paid to participate in this research study.

COSTS: You and/or your insurance company will be responsible for your routine scheduled endoscopy. The advanced imaging endoscopy procedure will add approximately 10 minutes to the procedure time of the already scheduled routine endoscopy. You will not be additionally charged for the advanced imaging endoscopy portion of your procedure which is part of the research study.

Sponsor: The National Institutes of Health, Olympus and Mauna Kea Technologies are providing financial support and/or material for this study.

CONTACT INFORMATION

Appointment Contact: If you need to change your appointment, please contact Dr. Shai Friedland at 650-493-5000 ext 64800.

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this **research study**, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Dr. Shai Friedland You may contact him now or later 650-493-5000 ext 64800. You should also contact him if you feel you have been hurt by being a part of this study.

Independent of the Research Team Contact: If you are not satisfied with the manner in which this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a research study subject, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

COMPENSATION

All forms of medical diagnosis and treatment -- whether routine or experimental -- involve some risk of injury. Should you be injured as a result of participation in this research project which has been approved by a VA Research and Development Committee and conducted under the supervision of one or more VA employees, VA will provide you free medical care for those injuries pursuant to 38 C.F.R. 17.85. This section applies to both Veteran and non-veteran research subjects. You will not be afforded medical care for: (1) treatment for injuries due to noncompliance by you with study procedures, or (2) research conducted for VA under a contract with an individual or a non-VA institution.

If you are a Veteran, 38 U.S.C.A. § 1151, may provide you with dependency and indemnity compensation for a qualifying additional disability or a qualifying death in the same manner as if such additional disability or death were service-connected. A disability or death is a qualifying additional disability or qualifying death if the disability or death was not the result of your willful misconduct and was caused by hospital care, medical or surgical treatment, or examination furnished to you and the proximate cause of the disability or death was either; (a) carelessness, negligence, lack of proper skill, error in judgment, or similar instance of fault on the part of the Department in furnishing the hospital care,

medical or surgical treatment, or examination; or (b) an event not reasonably foreseeable. For further information, contact the V.A. Regional Counsel at (415) 750-2288.

You do not waive any liability rights for personal injury by signing this form. If you feel that the above remedies for your injuries are not sufficient, and irrespective of your status as a Veteran or a non-veteran, the Federal Tort Claims Act, 28 U.S.C. §§ 1346(b) and 2671-2680, may provide an additional remedy if the VA is at fault for your injuries.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and
- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

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Signing your name means you agree to be in this study and that you will receive a copy of this signed and dated consent form.

_____ _____
Signature of Subject Date

_____
Print Name of Subject

Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent

HIPAA regulations require the participant to give separate written permission (signature) for the use of their protected health information.

Person Obtaining Consent HIPAA Authorization confirmation:

☐ Confirm the participant signed the VA HIPAA Authorization (VA 10-0493)