H-36538- ACCURACY, YIELD AND CLINICAL IMPACT OF A LOW-COST HIGH RESOLUTION MICROENDOSCOPE IN THE EARLY DIAGNOSIS OF ESOPHAGEAL ADENOCARCINOMA

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. Barrett's Esophagus occurs when stomach acids change the normal tissue lining the esophagus (the tube that carries food from the mouth to the stomach), to tissue that resembles the lining of the intestine. Barrett's Esophagus has a close association to esophageal adenocarcinoma (cancer that occurs in the esophagus). It has been reported to increase the risk of progression to esophageal adenocarcinoma by almost 40 to 125 times. Currently, surveillance endoscopy with 'random' four biopsies of flat mucosa (mucosa is moist tissue that lines certain parts of the inside of your body) and targeted biopsies of irregular mucosa is recommended for patients with Barrett's Esophagus to screen for esophageal adenocarcinoma every 6-36 months. Despite these recommendations, the result of this approach has been shown to be low, with up to 57% of neoplasia (the formation or presence of a new, abnormal growth of tissue) missed by these random' biopsies. In addition, a large number of normal biopsies are needlessly obtained increasing the cost and risk of the procedure. Thus, there is a great need for different plans that increase the effectiveness and yield of endoscopic surveillance. Confocal microendoscopy, a novel microscopic optical imaging style, has been shown to increase diagnostic yield significantly. However, existing confocal platforms are expensive and have a high learning curve which has prevented widespread use outside of a handful of academic centers. In a joint effort with Rice University, we have developed a low-cost, high-resolution microendoscope (HRME) that can be inserted through the biopsy port of any standard endoscope to provide subcellular, 1000x magnified images of the esophageal mucosa that resemble real-time histopathology (the study of changes in tissues caused by disease). Our theory is that such a device can enhance the effectiveness of endoscopic surveillance of Barrett's Esophagus. In a prior pilot study, we showed that when using the HRME with a topical fluorescent contrast agent, benign (noncancerous) mucosa could be distinguished from neoplasia with a negative predictive value of 95%. We feel this is very promising as it suggests that a normal 'optical' read could potentially eliminate the need for a tissue biopsy. Our plan is to compare standard endoscopy against HRME with standard endoscopy in an effort to see if this low-cost device can increase the accuracy and diagnostic yield of screening for cancer in patients with Barrett's Esophagus.

This research study is funded by National Cancer Institute

Purpose

The purpose of this study is to find out if the use of the high-resolution microendoscope (HRME) can help doctors see precancerous or cancerous tissue in patients with Barrett's esophagus. The HRME has a very powerful microscope which can magnify images of the inside of the esophagus. Barrett's esophagus is a precursor lesion (precancerous tissue) to a special type of cancer in the esophagus: esophageal adenocarcinoma. Esophageal cancer is the common cause of digestive cancer all over the world. Early detection is still regarded as the best method of improving survival from this disease and endoscopy is the most widely used technique for early detection and diagnosis. Endoscopy involves visual examination of the esophagus using a flexible, thin tube (endoscope) with a light and a small camera at the end. Such routine examination is important in patients with Barrett's esophagus. The HRME being used in this study is considered investigational because it has not been approved by the Food and Drug administration (FDA). The use of the probe also requires a contrast dye called

Proflavine to be sprayed on to the tissue in the esophagus to highlight abnormal areas. Proflavine is also considered investigational because it is not approved by the FDA.

You may qualify to take part in this research study because you have Barrett's esophagus and you are scheduled for a routine endoscopy or endoscopic treatment with biopsies.

Procedures
The research will be conducted at the following location(s):
Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC).

To perform an esophageal biopsy, a small amount of esophagus tissue is removed with a wire-shaped device that is inserted into the endoscope. It is considered routine to have areas that do not appear normal to be biopsied and to have 4 samples of tissue removed (1 from each of the 4 walls of the esophagus) every 1-2 cm (about the size of 1/2 - 1 pencil eraser) throughout the esophagus affected with Barrett's. No additional biopsies will be taken as part of this study.

If you agree to participate in this study, you will be randomized (assigned by chance, like a flip of a coin) for research purposes to one of the following methods for your upper endoscopy. You will not be told which study treatment you are getting, however your study doctor will know.

Group A: If you are in Group A, you will have a routine upper endoscopy with standard of care biopsies.

Group B: If you are in Group B, your esophagus will be imaged (pictures taken) with the HRME before the biopsies are taken. The procedures listed below are part of the routine standard of care for an endoscopy exam, except for the images that are being taken for Group B. The use of theHRME in this research will not change your standard of care procedures.

- You will be given general anesthesia (sleep medication).

-After you are under anesthesia, the following will take place for your standard of care procedure: endoscopy will be performed. The location and level of each abnormal area seen will be recorded.

-The following will take place for research purposes (Group B only): your esophagus will be sprayed with 10 ml (about 2 teaspoons) of proflavine. TheHRME (about the the width of a piece of spaghetti) will be inserted through the endoscope. The investigator will then look for an area of abnormal (damaged or precancerous) tissue and will take pictures.

-Group B only: microscopic images will be obtained of all areas before the standard of care biopsy is done.

-Standard of care biopsies will then be obtained.

-Group B: After all of the biopsies and imaging are done, the probe will be removed.

-You will be given the pathology results (a written explanation of what was found on the biopsy) of all tissue that was removed from your esophagus.

-Group B: You will not be given the imaging results.

-You will be contacted by the study doctor or the study coordinator within 2-5 days of your procedure to check for any side effects you may be experiencing.

Your samples will not be used for future genetic tests and no other test than those authorized will be performed on the biological sample.

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 and Baylor St. Luke's Medical Center (BSLMC) 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.
- Demographic information (name, D.O.B., age, gender, race, etc.)

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, Baylor St. Luke's Medical Center (BSLMC), 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.

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 and Baylor St. Luke's Medical Center (BSLMC) are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine and Baylor St. Luke's Medical Center (BSLMC) 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 and Baylor St. Luke's Medical Center (BSLMC) 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, and Baylor St. Luke's Medical Center (BSLMC) 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: Sharmila Anandasabapathy
One Baylor Plaza
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.

Proflavine: There is the possibility of a severe allergic reaction (anaphylaxis) to the Proflavine contrast dye in which the participant may have difficulty breathing and their blood pressure may drop. Proflavine may also cause irritation of the gastric mucosa (stomach lining) resulting in nausea and vomiting. Jaundice (yellowing of the skin or whites of the eyes) and serious toxic hepatitis (inflammation of the liver due to certain substances) may also be caused by the proflavine. There are procedures in place to treat the participant in the endoscopy room in the event that this happens. Proflavine is used at small

doses and we have not noticed any side effects to date related to this drug.

Specimen Imaging Probe: There are no known risks from the use of the High-resolution microendoscope (HRME).

Anesthesia: There may be additional risks from the added time of additional sedation, such as decreased blood pressure.

Aspiration (inhaling) of fluid into the lungs during endoscopy: This might cause inflammation in the lungs. Safeguards to prevent this from happening while you are under anesthesia will be in place during and after the procedure, and your breathing and other vital signs will be carefully monitored.

Biopsies
There is the possibility of some hoarseness, sore throat, difficulty and/or pain in swallowing, bleeding or infection, as well as discomfort at the surgical site.

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.

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.

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 Barrett's esophagus and esophageal adenocarcinoma. .

Alternatives
The following alternative procedures or treatments are available if you choose not to participate in this study: You may choose to just have the endoscopy and biopsies. In all cases you will receive appropriate medical care, including treatment for pain and other symptoms of Barrett's esophagus and esophageal adenocarcinoma..

Investigator Withdrawal of Subject from a Study

The investigator or sponsor may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city, if you do not take your study medication, or if you have a serious reaction to your study medication) or because the entire study is stopped. The sponsor, investigator, Food and Drug Administration, or Institutional Review Board may stop the study at any time.

Subject Costs and Payments

You and/or insurance company will be responsible for the costs of the endoscopy and the biopsies that are performed for standard of care. You will not be charged for the specialized imaging or the contrast sprays that are part of the research if you are randomized to Group B. Group A does not have additional research procedures.

You will not be paid for taking part in this study.

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.

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.

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: SHARMILA ANANDASABAPATHY at 713-798-8105 during the day and (713) 798-1000 and ask for the

gastroenterolgist (GI doctor) on call after hours.

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.

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