Official Title: Effectiveness and Performance of an Optical Biopsy Technology for Esophageal Cancer in Brazil and the United States

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H-53483- EFFECTIVENESS AND PERFORMANCE OF A MOBILE, AUTOMATED, OPTICAL BIOPSY TECHNOLOGY FOR ESOPHAGEAL CANCER SCREENING: A CLINICAL STUDY IN BRAZIL AND THE UNITED STATES

Concise and Focused Presentation

You're invited to join a research study. In this study, you'll have a procedure called upper endoscopy. This involves a long, bendy tube with a light and camera on the end being placed down your throat to check out your esophagus.

As part of our study, we'll use a special tool called an artificial intelligence-based mobile high-resolution microendoscope (AI-mHRME). Artificial intelligence is a computer program that can perform tasks that humans can do, and in this case, it takes extra pictures of the cells in your esophagus during the endoscopy. The program also identifies any abnormal cells to assist doctors in finding any unusual cells in your esophagus. Your participation is voluntary and a way to contribute to medical research.

During the AI-mHRME procedure, we use Proflavine Hemisulfate, a special dye, to see the cells in your esophagus. This dye is safe and easily washed away with water. A trained nurse assists the doctor by spraying your esophagus with Proflavine. Then, the AI-mHRME is inserted through the endoscope to take pictures of your esophageal cells. Using Proflavine and AI-mHRME shouldn't make the endoscopy riskier, and we take standard precautions to avoid any issues. The AI-mHRME imaging might make the procedure last 10-15 minutes longer.

By participating in this study, your doctor may better understand changes in your cells during the procedure, and the information we gather will help others in the future. You'll still get the usual endoscopy care if you decide not to join the study.

You won't have to pay for anything related to the study, including AI-mHRME and Proflavine dye. Also, you won't be paid for taking part in this study.

There are potential risks to the study procedures, some of which are mentioned below. There could be other risks we don't know about. Most side effects go away shortly after the endoscopy, but in rare cases, they could be severe, long-lasting, or even permanent, possibly leading to serious outcomes, including death. Let the study staff know about any side effects, even if you don't think they're connected to the procedure.

- Allergic Reaction: There's a rare chance of a severe allergic reaction to the Proflavine dye, which could cause difficulty breathing and a drop in blood pressure. If this happens, procedures are in place to treat participants in the endoscopy room. However, knowing that this group has used Proflavine before without any harmful events is reassuring.
- Specimen Imaging Probe: Using the imaging probe poses no known risks.
- Anesthesia: There may be risks due to the extra time spent under sedation, such as decreased blood pressure.
- Inhaling Fluid Into Lungs: Under anesthesia, there's a small risk of inhaling fluid into the lungs, which could cause lung inflammation. Precautions will be taken during and after the procedure, and vital signs will be carefully monitored. If a participant experiences symptoms not explained by the procedure, informing the study doctor is essential.

- Pregnancy: The use of Proflavine during pregnancy isn't well understood, and drugs can potentially harm the fetus. To ensure safety, all patients of child-bearing age will undergo a urine pregnancy test before the endoscopy, following standard hospital protocol. Any pregnant patient will be excluded from the procedure and the study.
- Loss of Privacy: To protect your privacy, the study will minimize the risk of sharing information by removing personal details and storing data securely. Study results and publications will be anonymous and won't include identifiable information.

The total duration of the research study will be 7 days. The first day will be the enrollment, consent, questionnaire, and endoscopy procedure. Seven days after the procedure, we will call you to ask how you are recovering from the procedure and if you have any problems. We may follow up a year later to see how you are doing and if you have any new diagnoses.

Background

You are invited to take part in a research study. Please read this information and feel free to ask any questions before agreeing to participate in the study.

Esophageal cancer is the 6th most common cause of cancer-related mortality worldwide. While esophageal squamous cell neoplasia (ESCN) carries a significant global burden, those in certain underserved geographic regions (South America, eastern Africa, eastern Iran, and northern China) have a particularly high number of new cases of ESCN (incidence) and number of people who die from ESCN (mortality rates) due to lack of endoscopic screening capacity. Endoscopy with Lugol s chromoendoscopy or digital chromoendoscopy has shown high sensitivity for screening (>95%) or how well it can correctly identify a person with ESCN. Lugol's chromoendoscopy has poor specificity (<60%), which is how well a test can correctly identify a person who does not have ESCN. Lastly, Lugol's generates false-positive results due to confounding inflammatory areas, meaning that other inflamed areas in the esophagus near the ESCN may skew the test results. As a result, standard-of-care endoscopy produces many unnecessary biopsies, increasing the risk and cost of endoscopic screening and surveillance.

Our team has studied this microscope (HRME) in both China and Brazil with artificial intelligence (AI) software that can tell whether the esophagus's lining has cancer. The AI is a computer software program that can perform a human task; in this study it was for identifying any cells that look abnormal in the esophagus. This software assisted doctors in seeing anything that was out of the ordinary in the esophagus lining. In these studies, we saw that 1 in 6 patients could walk out of the procedure without ANY biopsy, and almost 1 in 5 patients had their treatment plan changed correctly because of the HRME diagnosis. In addition, the use of the computer software with the HRME increased the confidence level of the doctors, which allowed the doctors to correctly treat, not treat, or biopsy 64% of the time. When these doctors were interviewed, they uniformly favored this computer-assisted HRME approach. However, some doctors were unsure how to get the equipment into their endoscopy centers for routine use in their patients. Since the computer-assisted HRME is currently in research studies, some doctors interviewed were unsure how the equipment could be purchased, used, and maintained in their clinical centers.

As part of research conducted with HRME, we use Proflavine Hemisulfate, a staining dye, to dye the esophagus where we see any abnormal areas to help us better see the cells when the probe is against the esophageal lining. Dr. Sharmila Anandasabapathy is the sponsor for this investigational drug, and it is safe to use inside the body. Proflavine is an antibacterial agent used as a topical antiseptic in wound dressings and umbilical cord care. As a liquid that can dye nucleic acids like DNA or RNA, which are genetic material found inside cells, proflavine is also an effective optical contrast agent for visualizing cell nuclei.

This research is funded by the National Institutes of Health (NIH).
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.

Purpose
This study aims to enhance and assess the impact of an artificial intelligence mobile high-resolution microendoscope (AI-mHRME) on diverse populations in the USA and Brazil. For this study, AI technology is a computer software program that can perform human tasks. It was developed to help look at the cells in the esophagus and tell doctors if any cells look abnormal.

We plan to enroll patients scheduled for routine endoscopy who are either under surveillance or screening for ESCN. The AI-mHRME probe will capture images of the esophagus in abnormal areas, and the doctor's diagnosis during the procedure will be determined. These images will be compared to the pathology results from collected biopsies.

A challenge in the community is that most doctors are unfamiliar with interpreting these microscopic HRME images. The research aims to test a computer software program designed to interpret these HRME images, aiding doctors in diagnosing high-risk patients undergoing LCE followed by HRME for esophageal cancer screening. We will compare the results of LCE to HRME and clinical interpretation. The goal is to develop a precise and swift diagnosis, enabling the use of this low-cost technology in low-resource or community settings and improving the care of patients at risk of developing esophageal cancer.

Procedures
The research will be conducted at the following location(s):
Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), and HCHD: Harris County Hospital District Ben Taub.

In Brazil, the research will be conducted at the following location(s): Instituto do Câncer do Estado de São Paulo (ICESP), São Paulo, Brazil; and Barretos Cancer Center Hospital de Amor (BCC), Barretos, Brazil.

1. Routine Endoscopy: As part of your standard care for esophageal cancer, we will collect images of

your esophagus during a standard upper endoscopy ordered by your physician. Additionally, body measurements such as BMI and waist circumference will be obtained as part of this standard procedure.

2. Research Procedure: The study procedure will begin following the routine endoscopic assessment. With the nurse's assistance, the doctor will spray your esophagus with 2 teaspoons (10 mL) of Proflavine Hemisulfate using a spray catheter. Proflavine is a safe staining dye for use in your esophagus. It will color the cells in the esophagus to make it easier for the doctor to see them for abnormalities. Next, the doctor will rinse the Proflavine with water from the endoscope. The sterile and disinfected AI-mHRME probe will then be inserted through the biopsy channel of the endoscope until it gently touches the esophageal lining. The AI-mHRME probe is attached to a computer where there is the AI software. This software allows the doctor to see the cells on the screen, and the software can produce a score that helps the doctor determine if there are any abnormalities. During this time, the doctor will move the AI-mHRME probe so that it can touch the esophagus wall and move it around to capture photos. The focus will be to look at any areas in the esophagus that may appear abnormal or irregular under Lugols chromoendoscopy (LCE, standard endoscopy) and AI-mHRME. This means these are areas where the iodine used in LCE did NOT stain. A study coordinator will collect data throughout this procedure, including the time and date of procedures, esophageal descriptions, doctor interpretations of LCE and AI-mHRME, LCE abnormal biopsy collection sites, etc.

3. Results and Follow-up: You will not receive the AI-mHRME imaging results. However, within 7 days of your procedure, the study doctor or coordinator will contact you to check for any side effects you may be experiencing.

4. Investigational Devices: The AI-mHRME, equipped with a powerful microscope, is considered investigational and not yet FDA-approved for general use. It has received an Investigational Device Exemption (IDE) from the FDA, allowing its use in the clinic for data collection and research. The AI-mHRME probe also requires using the investigational contrast dye Proflavine to enhance the visibility of abnormal areas in the esophagus. Proflavine is monitored under an FDA-approved investigational new drug (IND) status under Dr. Anandasabapathy's supervision at Baylor College of Medicine.

The total study participation period will be 7 days, starting from the day of your endoscopy procedure and ending with the 7-day follow-up phone call. We may call you again in a year to determine if you had any further diagnoses at a later time.

Clinically Relevant Research Results

The results generated from this research study are not expected to have any clinical relevance to you.

Sharing and Future Research Studies with Identifiable Private Information

Your identifiable private information collected as part of this research, even if the identifiers are removed, will not be used or distributed for future research studies.

Sharing and Future Research Studies with Identifiable Biospecimens

Your identifiable biospecimens collected as part of this research, even if the identifiers are removed, will not be used or distributed for future research studies.

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, Baylor St. Luke's Medical Center (BSLMC), and HCHD: Harris County Hospital District Ben Taub 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
- Demographic information (name, D.O.B., age, gender, race, etc.)
- 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, Baylor St. Luke's Medical Center (BSLMC), HCHD: Harris County Hospital District Ben Taub, NATIONAL CANCER INSTITUTE (NCI) and their representatives, 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, Baylor St. Luke's Medical Center (BSLMC), and HCHD: Harris County Hospital District Ben Taub are required by law to protect your health information. By signing this document, you authorize Baylor College of Medicine, Baylor St. Luke's Medical Center (BSLMC), and HCHD: Harris County Hospital District Ben Taub 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, Baylor St. Luke's Medical Center (BSLMC), and HCHD: Harris County Hospital District Ben Taub 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 CANCER INSTITUTE (NCI) and their representatives, 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, Baylor St. Luke's Medical Center (BSLMC), and HCHD: Harris County Hospital District Ben Taub 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. Sharmila Anandasabapathy, Neurosensory Center (NEUR) NA 105C 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

1. Allergic Reaction (Anaphylaxis): You may have a severe allergic reaction to the Proflavine contrast dye, resulting in difficulty breathing and a drop in blood pressure. If such a reaction occurs, we have procedures to treat you in the endoscopy room.

2. Specimen Imaging Probe (AI-mHRME): You will have minimal to zero risks when we use the imaging probe during the endoscopy procedure. No risks are associated with using the imaging probe (AI-mHRME).

3. Anesthesia: You may have additional risks due to the extended duration of sedation, potentially leading to decreased blood pressure. We have procedures to treat you in the endoscopy room.

4. Inhaling of Fluid into the Lungs (Aspiration) during Endoscopy: You may have a risk of lung inflammation if you inhale fluid in the lungs during the endoscopy procedure. While you are under anesthesia, we will implement safeguards to minimize the chances of this happening. We will meticulously monitor your breathing and vital signs for any alarming changes. If you experience any symptoms that the study doctor did not previously explain, you should notify the study team promptly.

5. Pregnancy: If you are pregnant (determined by urine test before the endoscopy procedure), you will be excluded from both the study and the endoscopy procedure. Standard hospital protocol includes a urine pregnancy test for all patients of child-bearing age before endoscopy. Insufficient information is available regarding the use of Proflavine in pregnancy, and drugs can have harmful effects on the fetus.

6. Loss of Privacy: There is the potential for the loss of confidentiality. You will give consent on the day of your endoscopy procedure in a private area. We will collect only essential information from you that is required for a standard surveillance endoscopy. You will be assigned an ID number for all forms, images, and communications to maintain anonymity. All your data will be coded and de-identified using this assigned study ID. Any documents with your Protected Health Information (PHI) will be redacted before being sent for data monitoring/entry. All your PHI that we collect for the study will be stored securely. We will minimize intrusion on your privacy. The only additional times we will contact you will be 7 days after the endoscopy procedure and one year later to follow up on your symptoms and check for adverse events. Only the study coordinator or the Principal Investigator will contact you for follow-up. Your participation in the study will only be discussed between you and the study team.

The risk to you is minimal for the post hoc image analysis project. Privacy concerns are addressed by assigning a unique, random ID to you and other participants, and we will not store identifying information.

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 changes in your cells during your scheduled procedure. This increased insight could contribute to developing more effective methods for detecting esophageal cancer in the future. Additionally, the knowledge gained from this research has the potential to benefit the general population by advancing our understanding of esophageal cancer detection methods and improving overall healthcare practices. Your participation is valuable in contributing to advancements that can positively impact medical care for others.

Alternatives

The following alternative procedures or treatments are available if you choose not to participate in this study: If you decide not to participate in the study, you will still receive the standard of care, and your scheduled endoscopy procedure will proceed as planned. Your medical care will remain the same, regardless of your decision to participate or not in the study. It is entirely your choice, and declining participation will not affect the quality or nature of the care you receive during the routine endoscopy ..

Subject Costs and Payments

Participating in this research will not incur any costs for you. The standard of care procedures, including the biopsy and endoscopy, are not covered by the study and will not be billed to you. The study will cover the costs associated with the AI-mHRME and Proflavine Hemisulfate.

You will not receive any payment for participating in this study. Your involvement is entirely voluntary and aims to contribute to valuable medical research. If you have any questions or concerns about the financial aspects of the study, please feel free to talk with the study coordinator or your healthcare provider.

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

Research Related Injury

All research activities will take place on-site in a hospital setting. In the event of any injuries, they will be managed according to the standard of care in a hospital setting. The research personnel will try to minimize, control, and treat any complications that may arise during this research.

If you experience an injury related to this study, the medical care you receive will be your responsibility or covered by your insurance, similar to any other medical care. The research team is committed to providing appropriate medical attention and managing adverse events following established medical practices. If you have any concerns or questions about this aspect of the study, feel free to discuss them with the study coordinator or your healthcare provider.

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 ADRIANNA MALIGA at 713-798-5987 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.

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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