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Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals

Protocol Number: H-36538
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Section Aa: Title & PI

A1. Main Title

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

A2. Principal Investigator

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A3a. Financial Conflict of Interest

Does any member of study personnel (Investigator (including investigator's spouse and/or dependent children)) that are involved in the design, conduct, or reporting of the research have a Significant Financial Interest (SFI) that would reasonably appear to be affected by the research for which funding is sought and/or associated with an entity/business that would reasonably appear to be affected by the research?

No

Section Ab: General Information

A4. Co-Investigators

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A5. Funding Source:

Organization: NATIONAL INSTITUTES OF HEALTH (NIH)

A6a. Institution(s) where work will be performed:

BCM: Baylor College of Medicine
Baylor St. Luke's Medical Center (BSLMC)

A6b. Research conducted outside of the United States:

Country:
Facility/Institution:
Contact/Investigator:
Phone Number:

If documentation of assurances has not been sent to the Office of Research, please explain:

A7. Research Category:

Cancer Related, Cancer - Adult

A8. Therapeutic Intent

Does this trial have therapeutic intent?
No

Section B: Exempt Request

B. Exempt From IRB Review

Not Applicable

Section C: Background Information

In the United States, almost 15 thousand people die from esophageal adenocarcinoma (EAC) every year. (Ries LAG, 2005). Barrett's Esophagus (BE) is a known precursor lesion that increases the risk of progression to EAC by 40 to 125 times. Despite this increased risk, specific biomarkers or imaging modalities to diagnose BE-associated dysplasia or neoplasia have yet to be completely developed. Therefore, currently, routine endoscopies remain the standard of care to detect early adenocarcinoma and dysplasia in BE patients. However, the sensitivity of standard white-light endoscopy with mucosal biopsy in diagnosing EAC in BE patients is less than 50% (Sharma). One of the reasons early EAC or BE-dysplasia is not picked up by standard endoscopy is that BE mucosa with dysplasia or early cancer is not endoscopically distinguishable from non-cancerous BE mucosa. Therefore, multiple biopsies (4-quadrant biopsies every 1-2 cm of BE

segments) are required to ensure that dysplasia or neoplasia is not missed. However, these extensive biopsy protocols lead to long procedure times and high costs while still missing dysplastic or neoplastic lesions. Moreover, the decision to perform an endoscopic mucosal resection cannot necessarily be determined until the histopathology is confirmed and a second endoscopy is performed. Our group, in collaboration with Rice University, has developed a low-cost (< $3,500), portable, battery-powered, high resolution microendoscope (HRME) that can be inserted through the biopsy channel of any standard endoscope. When used with 1-5 ml of topical proflavine hemisulfate 0.01%, a fluorescent contrast agent, the device provides subcellular images of esophageal epithelium and can delineate the cellular and morphologic changes associated with neoplastic progression of BE to low-grade neoplasia, high-grade neoplasia and finally to esophageal adenocarcinoma. Topical proflavine has been used in confocal imaging in Europe and Asia with no adverse events to date and is being used under an IND issued by the FDA (#102,217).

Preliminary ex-vivo data has been published in Gastrointestinal Endoscopy. This data confirmed that HRME images of Barrett's metaplasia and neoplasia could be correlated to gold standard histopathology. Moreover, our group recently conducted a small pilot study of HRME in a high risk BE population that demonstrated a sensitivity of 81% and a specificity of 85%. Most encouraging, however, was the negative predictive value of 95% that we achieved in this study. This suggests that areas that are deemed "non-neoplastic" on HRME may not need to be biopsied.

We believe that the next step in determining whether HRME can enhance the efficiency and yield of current surveillance is to perform a randomized, controlled trial comparing HRME to standard white light endoscopic protocol. Moreover, the in-vivo data we hope to collect will show that HRME will allow endoscopists to make informed real-time decisions regarding biopsies and endoscopic mucosal resections. Ultimately, we believe HRME can reduce the number of biopsies necessary as well as the total procedure time required to screen for BE-associated dysplasia and EAC. Therefore, HRME could reduce the overall cost of screening and become a much more attractive option for low-income communities.

As incidence rates for cancer rise, it is imperative that we improve early detection strategies. More importantly, it is critical that we develop cost-effective, robust platforms that can be used in community based screening/surveillance programs. We believe that successful results can be translated to other organ systems and, thus, help address the global costs of rising cancer incidence.

Section D: Purpose and Objectives

Our central hypothesis is that the low-cost HRME will increase the efficiency and yield of the current standard of endoscopic surveillance of BE. We believe the HRME will provide an in-vivo "optical biopsy" that will be comparable to gold standard histopathology and allow the endoscopist to make a more informed decision about whether to obtain a biopsy or even perform endoscopic therapy (i.e. endoscopic mucosal resection, EMR). Specific aims of this project are, in patients with known BE:

1a) to compare the diagnostic yield (defined as the proportion of mucosal biopsy samples with neoplasia) of HRME with directed biopsy to standard white-light endoscopy with 4-quadrant random biopsy (WL) for the diagnosis of BE-associated neoplasia in flat mucosa as well as mucosal lesions;

1b) to prospectively assess the potential clinical impact of HRME on the diagnosis and endoscopic surveillance of BE-associated neoplasia by determining if HRME alters the decision to obtain a mucosal biopsy or perform endoscopic mucosal resection (EMR) and changes the total number of total mucosal biopsies taken per procedure;

2) to determine the diagnostic accuracy (sensitivity, specificity, positive predictive value, negative predictive value) of HRME for the in-vivo diagnosis of neoplasia in a surveillance population of patients with BE using histopathologic diagnosis of mucosal biopsies as the reference standard;

3) to compare the total procedure time for imaging and mucosal biopsy acquisition of HRME with WL, stratified by length of BE (less than 3 cm and greater than 3 cm) and to determine the average HRME imaging time.

Section E: Protocol Risks/Subjects

E1. Risk Category

Category 3: Research involving greater than minimal risk and no prospect of direct benefit to the individual subject, but likely to yield generalizable knowledge about the subject's disorder or condition.

E2. Subjects

Gender:
Both

Age:
Adult (18-64 yrs)

Ethnicity:
All Ethnicities

Primary Language:
English

Groups to be recruited will include:
Patients

Which if any of the following vulnerable populations will be recruited as subjects?

Vulnerable populations require special protections. How will you obtain informed consent, protect subject confidentiality, and prevent undue coercion?

E3. Pregnant woman/fetus

Will pregnant women and/or fetuses (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E4. Neonates

Will neonates of uncertain viability or nonviable neonates (as described in 45 CFR 46 Subpart B) be enrolled in the research?
No

E5. Children

Will children be enrolled in the research?
No

Section F: Design/Procedure

F1. Design

Select one category that most adequately describes your research:
u) Drug, Phase II, Single Center

Discuss the research design including but not limited to such issues as: probability of group assignment, potential for subject to be randomized to placebo group, use of control subjects, etc.
The patient will be assigned to one of two groups: Group A: high resolution white-light endoscopy followed by random biopsy (WL) or Group B: high resolution white-light endoscopy plus HRME followed by directed mucosal biopsy (HRME). Randomization assignments (WL vs. HRME) will be computer-generated with allocation concealment using sealed envelopes.

Inclusion Criteria:
All consecutive outpatients with > 1 cm biopsy-proven Barrett's Esophagus who are undergoing standard of care endoscopic surveillance for metaplasia, dysplasia, or neoplasia.

Exclusion Criteria:
• Allergy or prior reaction to the fluorescent contrast agent proflavine • Patients who are unable to give informed consent. • Known advanced adenocarcinoma of the distal esophagus, or dysplastic/suspected malignant esophageal lesion greater than 2 cm in size not amenable to EMR • Patients with a history of a severe allergic reaction (anaphylaxis) • Patients unable to undergo routine endoscopy with biopsy : • Women who are pregnant or breastfeeding • Prothrombin time greater than 50% of control; PTT greater than 50 sec, or INR greater than 2.0 • Inability to tolerate sedated upper endoscopy due to cardiopulmonary instability or other • Patients with known, untreated esophageal strictures, prior partial esophageal resection, or altered anatomy preventing passage of the endomicroscope • Patients with known severe esophagitis • Patients with suspected but no biopsy confirmed BE

F2. Procedure

Written informed consent will be obtained prior to study participation using the IRB-approved consent form. Identifying information collected includes D.O.B., age, gender, race and date of encounter. The patient will be assigned to one of two groups: Group A: high resolution white-light endoscopy followed by random biopsy (WL) or Group B: high resolution white-light endoscopy plus HRME followed by directed mucosal biopsy (HRME). Randomization assignments (WL vs. HRME) will be computer-generated with allocation concealment using sealed envelopes.

White Light Endoscopy (WL) Procedure (Group A)

Patients assigned to the WL group will undergo careful standard examination of the upper GI tract with a standard high resolution endoscope (Olympus Corporation) without HRME. Endoscopic landmarks and BE characteristics will be described as listed in the previous section. Any mucosal lesions in the BE will be classified using the Paris classification. The endoscopist will predict whether BE and dysplasia are present based upon the white light endoscopic findings (endoscopic diagnosis) and whether neoplasia is suspected if there are any endoscopic lesions (endoscopic plan).

Mucosal biopsies of any discrete lesions will be obtained and placed in separate pathology containers per standard of care. Then, four-quadrant mucosal biopsies of the flat BE mucosa (a biopsy from each quadrant of the BE at each level) will be taken per standard of care: every 1 cm (for patients with suspected neoplasia) or every 2 cm (for patients undergoing routine surveillance), starting at the GE junction, moving proximally to the squamocolumnar junction. These mucosal biopsies will be obtained. in a similar fashion to the standard Seattle biopsy protocol4. This biopsy protocol is commonly used for obtaining surveillance biopsies to sample representative areas of the entire length of the BE. Each level of the biopsies designated by the distance (in centimeters) on the endoscope from the patient's gums.

The total time of the procedure, as well as the time needed to complete the standard endoscopy and the time needed to take tissue biopsies, will be recorded. The co-investigator or research coordinator will indicate the biopsy number and location of the biopsy on a standardized BE map. The biopsies from each site will be placed in formalin and labeled according to the biopsy location.

Post-procedure, the endoscopist will inspect the map created by the coordinator and approve the data recorded. The number of biopsies obtained and biopsy specimen bottles sent for processing will be tracked to allow calculation of pathology costs.

High Resolution Microendoscopy (HRME) Procedure (Group B)

All patients who fit the study criteria will be consented for HRME with biopsy and possible EMR (similar to colonoscopy with possible polypectomy). Examination of the esophagus, stomach, and small intestine with standard endoscopy will be performed using a high resolution video endoscopy (Olympus). The level of the gastroesophageal (GE) junction will be recorded. The level of the squamo-columnar junction (Z line) will also be recorded. Any proximal displacement of the Z line or gap between the GE junction and Z line will normally raise the suspicion for BE due to the presence of columnar mucosa in the distal esophagus. The maximum length of suspected BE (i.e. distance between the GE junction and Z line) and pattern of the BE (islands, tongues, circumferential columnar epithelium) will be recorded and photographed. A description of the BE using the Prague C&M criteria, which is used to describe the maximal length of BE and extent of circumferential BE, will also be recorded {Sharma, 2006 #4178}. Esophagitis will be described using the Los Angeles classification. The size, morphology, and location in the esophagus of every macroscopically visible lesion will be recorded and described using the 2002 Paris Endoscopic Classification of neoplastic lesions. The height of the mucosal lesion will be assessed by comparison with the diameter of a closed biopsy forceps (2.5 mm) {, 2003 #4280}.

After the endoscopic examination, the endoscopist will provide an endoscopic diagnosis for any visible mucosal lesions (pre-HRME diagnosis: i.e. neoplastic vs. non-neoplastic) and a plan for management during the procedure, such as biopsy or endoscopic mucosal resection (pre-HRME plan). These will be recorded prior to the initiation of HRME imaging.

For the HRME portion of the exam, 5-10 ml of proflavine hemisulfate (0.01%) will be sprayed on the esophageal mucosa. Proflavine is being used under an IND from the FDA (#102217). The HRME itself is an IDE exempt device per the FDA. The HRME will then be inserted through the biopsy channel of the endoscope and gently placed against the mucosa. The endoscopist will image each WL-discrete lesion first from the most distal to the most proximal. For each HRME imaged site, an optical read will be obtained (neoplastic vs. non-neoplastic) followed by a tissue biopsy of the imaged areas.

Following the targeted biopsies, random four-quadrant biopsies of the flat BE mucosa will be taken with every 1 cm (for patients with suspected high grade dysplasia (HGD)) or every 2 cm (for patients undergoing routine surveillance), starting at the GE junction, moving proximally to the Z line per standard of care. Prior to the standard tissue biopsy, an HRME read will be obtained from the area (neoplastic vs. non-neoplastic). A superficial dimple will be made with the HRME of each imaged site to "mark" the imaged area for biopsy. The latter is commonly performed in imaging correlation studies and has not been shown to affect pathology.

Pathology

The fixed biopsies will be oriented/embedded in paraffin and sectioned to facilitate comparison between histology and HRME images. Afterwards the serial sections will be routinely stained with hematoxylin and eosin for histopathologic examination.

The biopsies or resected specimens (from EMR) obtained from the examined areas will be routinely processed and interpreted by a single expert gastrointestinal pathologist in a blinded fashion and graded according to the Vienna Classification. The pathologist will provide a diagnosis for each biopsy specimen in the cassette to allow correlation with the endoscopic and HRME findings. The histopathologic diagnosis for each biopsy will be recorded on a standardized data collection form.

Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 47 Worldwide: 100

Please indicate why you chose the sample size proposed:

Approximately 100 subjects with 50 in the WL-arm and 50 in the HRME-arm. We anticipate that 15-20% of subjects may be not complete their endoscopy for various reasons (lack of biopsies, loss of Barrett's mucosa, visualization of a lesion > 2 cm, inability to complete endoscopy, etc.) which would allow 40 in each arm. Since each patient only requires one visit for enrollment into the study, we expect that 80 patients will be enrolled and randomized and complete the study.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

In this trial, the randomization will be stratified by risk group: high risk and average risk. All analyses described below will be stratified as well.

The primary outcome of the randomized trial is Diagnostic Yield, defined as the proportion of all biopsies that are truly neoplasia after histopathological review. A generalized linear model for logistic regression with multiple correlated binary outcomes within each patient will be used for data analysis (McCullagh and Nelder, 1989). In this model the binary outcome for each biopsy specimen is whether the specimen is classified as neoplasia or non-neoplasia, and the explanatory variable is the biopsy protocol group (Group A is standard of care, the control group; Group B is the optical biopsy protocol with HRME). PROC GLIMMIX in SAS will be used because of the correlations among samples from the same patient. The model will allow for testing whether the proportion of samples classified as neoplasia differs between the two biopsy protocols. The analysis will be stratified by risk group --- High Risk and Average Risk. A secondary outcome will be the estimation of the accuracy of each biopsy protocol. Because of the small numbers of true neoplasia patients that are expected to be present among patients enrolled in the trial, sensitivity on a patient-basis will not be estimated. However, specificity will be estimated, stratified by risk group, for each of the two biopsy protocols, along with a one-sided 95% confidence interval

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

Possible risks associated with the study procedures are listed below. There may also be risks that are not known. 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 the participant tell the study staff about any side effects that he/she may have had even if he/she does 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 gastric mucosa resulting in nausea and vomiting. Jaundice and serious toxic hepatitis may also occur. There are procedures in place to treat the participant in the endoscopy room in the event that this happens. Proflavine enhances visualization of the cell nuclei, because of the very low doses used, we have not noted any clinical sequelae or side effects related to the drug.

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

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 the participant is under anesthesia will be in place during and after the procedure, and participant's 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 the participant experiences any symptoms other than those that the study doctor has informed the participant are associated with the procedure, please let the study doctor know.

There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk.

H2. Data and safety monitoring plan

Do the study activities impart greater than minimal risk to subjects?
Yes

NOTE: The answer to the questions in H2 requires the completion of the form: 'Section H – Data and Safety Monitoring Plan' as an attachment in Section S.

H3. Coordination of information among sites for multi-site research

Is the BCM Principal Investigator acting as the SPONSOR-INVESTIGATOR for this multi-site research?
No or Not Applicable

Is BCM the COORDINATING CENTER for this multi-site research?
No or Not Applicable

Section I: Potential Benefits

Describe potential benefit(s) to be gained by the individual subject as a result of participating in the planned work.
There may be potential benefit to the individual participant for undergoing HRME as dysplasia may be identified by the procedure. All medical management decisions will be based upon the standard endoscopic and pathologic diagnoses.

Describe potential benefit(s) to society of the planned work.
The original purpose of this research was to provide a low-cost, portable endoscopic tool that can advance the screening of esophageal adenocarcinoma in BE patients. As incidence rates for cancer rise, it is imperative that we improve early detection strategies. More importantly, it is critical that we develop cost-effective, robust platforms that can be used in community based screening/ surveillance programs. We believe that successful results can be translated to other organ systems and, thus, help address the global costs of rising cancer incidence

Do anticipated benefits outweigh potential risks? Discuss the risk-to-benefit ratio.
The incremental risks of HRME with proflavine, added to the SOC white light with Lugol's iodine are minimal. White light endoscopy is standard of care and all subjects will be undergoing this SOC procedure.

Section J: Consent Procedures

J1. Waiver of Consent

Will any portion of this research require a waiver of consent and authorization?
Yes

Please describe the portion of the research for which a waiver is required. (Example: chart review to determine subject eligibility)
We will screen gastroenterology and endoscopy clinic schedules at BSLMC to identify current patients who may be eligible for participation in our clinical trial. Eligible subjects approved by a GI physician will then be contacted via telephone to determine participation interest, followed up by written, in-person consent prior to the procedure.

Explain why the research and the use or disclosure of protected health information involves no more than minimal risk (including privacy risks) to the individuals.
We will only store minimally required information on individuals who meet our inclusion and exclusion criteria. This information will be stored electronically behind BCM's firewall, and only research staff on a need to know basis will have access to the list. We don't believe this chart review will present additional privacy risk beyond routine patient care including use of electronic medical records.

Explain why the waiver will not adversely affect the privacy rights and the welfare of the research subjects.
The subjects we are screening for this clinical trial include current patients at BSLMC gastroenterology and endoscopy clinics who are already scheduled for medical care with the treating physicians on this protocol. Therefore, we don't believe the chart review presents an unjustified review of medical information. Subjects who satisfy the initial inclusion criteria screen, but who do not wish to participate after discussing over the phone, are not contacted for participation in the trial in the future, nor would it affect their ongoing medical care with their current physician.

Explain why the research could not practicably be conducted without the waiver and could not practicably be conducted without access to and use of the protected health information.
Our trial requires screening patients for study enrollment. We believe the chart review of current patients offers an efficient process for identification of subjects for the clinical trial. The known alternatives would depend on physician recruitment and referral or for subjects to self-identify to research staff based on advertising, both of which might contribute to slower accrual.

Describe how an adequate plan exists in order to protect identifiers from improper use and disclosure.

Only members of the research team on a need to know basis will have access to the list of potential research subjects. This list will include only the minimum required information and will be stored electronically behind BCM's firewall.

Describe how an adequate plan exists in order to destroy identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law.

Information on individuals on the list who satisfy the inclusion and exclusion criteria, but who state they are not interested in participating in the trial, will be deleted. We will only retain the most basic identifying information on individuals so that they are not contacted again in the future regarding trial participation. Similarly, information on individuals who do participate in the trial will also be limited so that we will not screen their records again in the future. At the conclusion of the trial, the list will be permanently deleted.

Describe how adequate written assurances exist in order to ensure that the PHI will not be reused or disclosed to (shared with) any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of the PHI would be permitted under the Privacy Rule.

Only research staff on a need to know basis will have access to the list. At present, this includes the Clinical Research Manager, research coordinator, and the GI physician. Research staff with access to this list have completed all human subjects and HIPPA training and are aware of human subjects protections in place and also understand the repercussions for improper use of such information. The information collected will only be used for the current trial, will not be shared with any outside party, will be stored with only the minimum required information behind the BCM firewall, and will be deleted at the earliest opportunity.

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.

Yes

Specific information concerning alcohol abuse:

No

Specific information concerning drug abuse:

No

Specific information concerning sickle cell anemia:

No

Specific information concerning HIV:

No

Specific information concerning psychiatry notes:

No

Demographic information (name, D.O.B., age, gender, race, etc.):

Yes

Full Social Security #:

No

Partial Social Security # (Last four digits):

No

Billing or financial records:

No

Photographs, videotapes, and/or audiotapes of you:

No

Other:

No

Will additional pertinent information be provided to subjects after participation?

No

If No, explain why providing subjects additional pertinent information after participation is not appropriate.

The information collected would include demographics and relevant clinical data. It would not include any additional information that could not be accessed by the patients through their own review of their medical record.

J1a. Waiver of requirement for written documentation of Consent

Will this research require a waiver of the requirement for written documentation of informed consent?

No

J2. Consent Procedures

Who will recruit subjects for this study?

PI

PI's staff

Describe how research population will be identified, recruitment procedures, any waiting period between informing the prospective participant and obtaining consent, steps taken to minimize the possibility of coercion or undue influence and consent procedures in detail.

Study subjects will be recruited from the PI's practice. Participation in the trial will be discussed with patients at a routine office visit prior to their endoscopy or on the day of their exam prior to endoscopy by the study investigator or Research Coordinator. The Research Coordinator will provide the patient with information regarding the trial that is being conducted. The patient will have an opportunity to review information and have all questions answered. The patient will decide whether or not he wants to participate in the trial by signing the informed consent form. Informed consent will be signed on the day of the scheduled endoscopic procedure. A waiver has been requested for the screening of subject charts prior to approaching them for participation in the trial.

Are foreign language consent forms required for this protocol?

Yes

Which of the following ways will you document informed consent in languages other than English?

Short-Form consent documents

J3. Privacy and Intrusiveness

Will the research involve observation or intrusion in situations where the subjects would normally have an expectation of privacy?

No

J4. Children

Will children be enrolled in the research?

No

J5. Neonates

Will non-viable neonates or neonates of uncertain viability be involved in research?

No

J6. Consent Capacity - Adults who lack capacity

Will Adult subjects who lack the capacity to give informed consent be enrolled in the research?

No

J7. Prisoners

Will Prisoners be enrolled in the research?

No

Section K: Research Related Health Information and Confidentiality

Will research data include identifiable subject information?

Yes

Information from health records such as diagnoses, progress notes, medications, lab or radiology findings, etc.

Yes

Specific information concerning alcohol abuse:

No

Specific information concerning drug abuse:

No

Specific information concerning sickle cell anemia:

No

Specific information concerning HIV:
No

Specific information concerning psychiatry notes:
No

Demographic information (name, D.O.B., age, gender, race, etc.):
Yes

Full Social Security #:
No

Partial Social Security # (Last four digits):
No

Billing or financial records:
No

Photographs, videotapes, and/or audiotapes of you:
No

Other:
No

At what institution will the physical research data be kept?
Baylor College of Medicine

How will such physical research data be secured?
Physical data will be stored in a locked file cabinet at all times in the PI's or Research manager's locked office.

At what institution will the electronic research data be kept?
Baylor College of Medicine

Such electronic research data will be secured via BCM IT Services- provided secured network storage of electronic research data (Non-Portable devices only):
Yes

Such electronic research data will be secured via Other:
Yes, (describe below):
Laptops will all be password protected. All files will be de-identified.

Will there be anyone besides the PI, the study staff, the IRB and the sponsor, who will have access to identifiable research data?
No

Please describe the methods of transmission of any research data (including PHI, sensitive, and non-sensitive data) to sponsors and/or collaborators.
Transmission will be done through secure/encrypted e-mail.

Will you obtain a Certificate of Confidentiality for this study?
No

Please further discuss any potential confidentiality issues related to this study.
n/a

Section L: Cost/Payment

Delineate clinical procedures from research procedures. Will subject's insurance (or subject) be responsible for research related costs? If so state for which items subject's insurance (or subject) will be responsible (surgery, device, drugs, etc). If appropriate, discuss the availability of financial counseling.
Neither the subject nor subject's insurance will be responsible for research related costs. Research related costs are specifically the use of the Proflavine and the use of the imaging probe if subjects are randomized to the HRME after the standard of care Lugol's + upper endoscopy. The costs related to the clinically indicated upper endoscopy are not research and are covered by the subject or their insurance.

If subjects will be paid (money, gift certificates, coupons, etc.) to participate in this research project, please note the total dollar amount (or dollar value amount) and distribution plan (one payment, pro-rated payment, paid upon completion, etc) of

the payment.

Dollar Amount:
0

Distribution Plan:

Section M: Genetics

How would you classify your genetic study?

Discuss the potential for psychological, social, and/or physical harm subsequent to participation in this research. Please discuss, considering the following areas: risks to privacy, confidentiality, insurability, employability, immigration status, paternity status, educational opportunities, or social stigma.
there is no genetic component to this study.

Will subjects be offered any type of genetic education or counseling, and if so, who will provide the education or counseling and under what conditions will it be provided? If there is the possibility that a family's pedigree will be presented or published, please describe how you will protect family member's confidentiality?

Section N: Sample Collection

SAMPLE: Tissue

What is the purpose of the sample collection?
Tissue obtained by biopsy will be collected for clinical diagnosis. No tissue or samples are collected only for research. The slides/tissue blocks used for a clinical diagnosis will be available for re-review by the pathologists to confirm a final study diagnosis.

For blood draws, specify the amount drawn, in teaspoons, at each visit and across the course of the subjects entire participation time.
n/a

Is there the possibility that cell lines will be developed with this sample?No

Sample will be obtained from:
Pathology

Will the sample be stripped of identifiers?
No

If sample will be released outside the hospital:

Will sample be released to anyone not listed as an investigator on the protocol? Will the information be identifiable, coded or de-identified?
Slides will be coded with the subject ID

Will sample material be sold or transferred to any third parties? Will the information be de-identified?
The slides will be loaned to MSSM for central review without PHI (coded only). They will be returned to BCM after review at MSSM.

If sample will be banked for future use:

Where will the sample be banked and for how long?
no

Does the banking institution have an approved policy for the distribution of samples?
n/a

If the entire sample will NOT be used during the course of this research study:

Will the remaining tissue be discarded? If not what will be done with the remaining sample after study completion and how long will the sample be kept?
n/a

Will samples be made available to the research subject (or his/her medical doctor) for other testing?
No

If a subject withdraws from the study:

Will subject have the option to get the remaining portion of their sample back?
No

Will samples be destroyed? If not, will they be kept anonymously? What will happen to the sample if the subject revokes authorization?
n/a

Will data obtained from their sample be deleted? What will happen to the sample if the subject revokes authorization?
n/a

Will study data or test results be recorded in the subject's medical records?
No

Will results of specific tests and/or results of the overall study be revealed to the research subject and or his/her doctor?
n/a

Please identify all third parties, including the subject's physician, to receive the test results.
n/a

Section O: Drug Studies

Does the research involve the use of ANY drug* or biologic? (*A drug is defined as any substance that is used to elicit a pharmacologic or physiologic response whether it is for treatment or diagnostic purposes)
Yes

Does the research involve the use of ANY gene transfer agent for human gene transfer research?
No

O1. Current Drugs

Drug : Proflavine Hemisulfate

Is this study placebo-controlled?
No

Will the research involve a radioactive drug that is not approved by the FDA?
No

Section P: Device Studies

Does this research study involve the use of ANY device?
Yes

Device 1: HRME

Section Q: Consent Form(s)

Accuracy, Yield and Clinical Impact of a Low-Cost High Resolution Microendoscope in the Early Diagnosis of Esophageal Adenocarcinoma

Section R: Advertisements

None