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Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

Sponsor: National Cancer Institute

Principal Investigator(s): Amitabh Chak MD

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio and the broader United States. This study is being offered at University Hospitals Cleveland Medical Center University Hospitals Ahuja Medical Center, University Hospitals Westlake Surgery Center, University Hospitals North Ridgeville Medical Center, and University Hospitals St Johns Medical Center in Northeast Ohio.

Key Information: The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?
We invite you to take part in a research study because you have some risk factors for a condition called Barrett's esophagus that can only be diagnosed by performing upper endoscopy.

What should I know about a research study?
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The purpose of this study is to develop a method to detect Barrett's esophagus in individuals with a new office based diagnostic test. Barrett's esophagus is a condition in which the flat pink lining of the swallowing tube that connects the mouth to the stomach (the esophagus) becomes damaged by acid reflux. It is associated with an increased risk of developing esophageal cancer.
Up to 400 adults who have risk factors for Barrett's esophagus but do not have chronic heartburn or regurgitation will be enrolled in this study at several different regional hospitals: University Hospitals (UH) Cleveland Medical Center, UH Ahuja Medical Center, UH Westlake Surgery Center, UH North Ridgeville Medical Center and UH St John Medical Center.

You are being asked to participate in this research study because you have some risk factors for a

condition called Barrett's esophagus which can only be diagnosed by performing upper endoscopy (the insertion of a long, flexible tube into your nose or mouth using a tiny camera on the end to see your upper digestive system).

Your treating doctor may also be an investigator on this research study. If so, your doctor will have an interest in both your welfare and in the research study. You are not required to take part in this research study. If you choose not to be in this study, the quality of your regular medical care will not be affected.

The following investigators: Dr. Amitabh Chak, Dr. Sanford Markowitz, and Dr. Joseph Willis are inventors of and consultants for the device and the markers used in this study which have been licensed to Lucid Diagnostics. These investigators receive payment from Lucid Diagnostics.

Dr. Helen Moinova, a researcher on the study team, has a financial interest in the manufacturer of the technology, Lucid Diagnostics. This disclosure is made so that you can decide if this relationship will affect your willingness to participate in this study.

There is a Case Western Reserve University institutional conflict of interest due to their ownership of the capsule balloon technology (the licensed investigational product).

Study investigators other than those listed above, will ensure you receive all study related information and determine your ability to be included in the research. These investigators and/or study coordinators will additionally perform the informed consent process with you. This disclosure is made so that you can decide if the financial relationships mentioned above will affect your willingness to be in this study.

If you have any questions regarding conflicts of interest, please ask your study doctor or call the University Hospitals Institutional Review Board at [redacted].

Please ask any questions you may have about the study or this consent form before signing it. Please take your time to make your decision. You will be given a copy of this form to keep.

How long will the research last and what will I need to do?

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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- Your participation in this study will include your completion of a questionnaire (which includes a series of measurements of your height, weight, waist and hip circumference). It should take about 5 to 15 minutes to complete. If you are uncomfortable or do not wish to answer a question on the questionnaire, you are welcome to skip-it and go on to the next question.
- Additionally you will undergo the performance of the EsoCheck procedure to donate tissue for the Esoguard Assay to analyze your tissue sample and a possible voluntary upper endoscopy.
- More detailed information about the study procedures can be found under "What extra tests and procedures will I have if I take part in this study?"

Is there any way being in this study could be bad for me?
There is a risk of breach of confidentiality of the study questionnaire. A concerted effort will be made to ensure that information about you is kept strictly confidential. All of your data and samples will be identified with a study code.

More detailed information about the risks of this study can be found under "What possible risks can I expect from taking part in this study?"

What possible benefits can I expect from taking part in this study?
We cannot know if you will have any benefit as a result of your participation in this study; this study may have potential benefits to you as a participant. If Barrett's esophagus is found, early detection and/or prevention of esophageal cancer may be of help to you. Your participation in this study will help to obtain information about treating subjects with Barrett's esophagus in the future. All information that is obtained from this study will be used scientifically.

What is the usual approach to detection of Barrett's esophagus?
Doctors often recommend an upper endoscopy to detect Barrett's esophagus in adults over age 50 who have chronic heartburn or regurgitation especially if the adults are white males who smoke or are overweight as these are all factors that increase the risk for Barrett's esophagus and esophageal cancer. By performing upper endoscopy and detecting Barrett's esophagus doctors can put patients in a surveillance program with a goal of preventing esophageal cancer or detecting it early. Although you have some risk factors for Barrett's esophagus your primary physician has not referred you for upper endoscopy because you do not have chronic heartburn or regurgitation. Upper endoscopy is generally not recommended unless you have those symptoms because upper endoscopy is expensive and there is a small but real chance of adverse events.

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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What are my other choices if I do not take part in this study?
If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available

Detailed Information: The following is more detailed information about this study in addition to the information listed above.

Questionnaire
Your participation in this study will include your completion of a questionnaire (which includes a series of measurements of your height, weight, waist and hip circumference). It should take about 5 to 15 minutes to complete. If you are uncomfortable or do not wish to answer a question on the questionnaire, you are welcome to skip-it and go on to the next question.

Release of Medical Information and Samples
Medical records may be required to confirm your medical history. You will be asked to sign a release of medical information for your relevant medical records and, potentially, the fixed tissue collected if you subsequently undergo upper endoscopy.

Capsule Balloon Test (EsoCheck)
You will be asked to undergo a capsule balloon test prior to your scheduled procedure. The capsule balloon test called EsoCheck (Lucid Diagnostics) is a new FDA approved method that is office-based and examines the esophagus without using sedative medications or an endoscope. This will be done as a research procedure.

The capsule balloon test will be performed by a qualified coordinator who has been trained in performing the procedure. While you are awake, the back of your throat may or may not be sprayed with a numbing medicine or, you may be asked to swallow a numbing medicine. You will then be asked to swallow the soft, plastic capsule attached to tubing that allows it to be pulled out. It will be deflated (no air in the capsule). After the capsule is swallowed, it will then be inflated (filled with air like a balloon) and withdrawn to collect a tissue sample from the bottom of your esophagus

The capsule will then be completely deflated and withdrawn (taken out) from your throat. This whole test should take about 5-10 min.

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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For your visit today, these are the only procedures the researchers are asking of you.

Diagnostic Test for Barrett's Esophagus (EsoGuard)

The sample from your esophagus collected by the EsoCheck capsule balloon will be sent to the laboratory for an EsoGuard test, which is a laboratory developed test that has an accuracy of 90% for Barrett's esophagus. The results of the test may not be available for several weeks. When the results become available you and your physician will be contacted by the study investigators with the results of the test.

If the EsoGuard test comes back positive suggesting that you may have Barrett's esophagus, you will have the option of scheduling and undergoing an upper endoscopy with esophageal biopsy to confirm whether you do or do not have Barrett's esophagus. You and your insurance will be billed for this upper endoscopy. An upper endoscopy for someone with a positive EsoGuard test is not considered a research test. Individuals who have Barrett's esophagus are recommended to have upper endoscopy every three years or more frequently if there are atypical cells to survey the esophagus and prevent cancer.

If the EsoGuard test comes back negative then the study investigators may offer you a research upper endoscopy for which you and your insurance will not have to pay. This will be considered a research test. You can decline to undergo a research upper endoscopy if you wish.

Upper Endoscopy

If you undergo an upper endoscopy, the procedure itself should take approximately twenty minutes. After you receive medication to numb the back of your throat, you will be sedated and the procedure will be performed with an endoscope (a long, thin flexible tube inserted into your body with a tiny camera at the end). Routine care biopsies (not for research) may be taken if Barrett's esophagus is identified during endoscopy. If you are found to have a normal esophagus or Barrett's esophagus, up to 12 additional brushings or biopsies will be obtained for research purposes.

What possible risks can I expect from taking part in this study?

Your participation in this study may involve the following risks. The Principal Investigator and

his research team have taken steps to minimize the expected risks but your participation in this study involves only slight risks. We cannot predict all risks or potential side effects in all subjects, It is important that you tell the researchers about any injuries, side effects, or other problems that you experience during this study.

Capsule Balloon Test

There may be mild discomfort while swallowing the capsule. Passage of the capsule through the throat and the attached tubing may stimulate choking or gagging in some patients. You may experience a transient chest pressure or pain sensation when the capsule is inflated like a balloon and pulled into the esophagus.

If the capsule is not withdrawn after you swallow it, there is an additional small risk of the capsule getting stuck in your intestine. There may be a very small risk of bleeding or perforation with a device in your esophagus.

Upper Endoscopy

Risks and discomforts associated with the upper endoscopy procedure include gagging, nausea, vomiting, sore throat, possible reaction to the numbing medicine for the back of your throat used during the procedure, and poking a hole in the lining of the esophagus (if this were to occur, it may require surgery to repair). In extremely rare cases, there is a risk of death associated when undergoing an endoscopy. The risk of death from this procedure is very low (1 in every 25,000 procedures).

The biopsy procedure is a standard part of clinical care. Risks and discomforts associated with the biopsies include increased bleeding and the possibility of poking a small hole (perforation) in the esophagus that would require surgery to repair. The risks associated with the use of a sedative drug include a possible slowing of breathing, drop in blood pressure, drowsiness and dizziness. If you have a standard upper endoscopy with sedation, you will remain in the recovery area and will be observed following the procedure to assure that no complications arise and until the sedation has worn off. You will not be permitted to drive after the procedure and will need someone to drive you home.

Breach of Confidentiality

Another risk is the breach of confidentiality of the questionnaire. A concerted effort will be made to ensure that information about you is kept strictly confidential. All data and samples will be identified with a study code.

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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What happens to the information collected for the research?
If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or distributed to another investigator for future research studies without your additional informed consent.

Can I stop taking part in this study?
Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:
- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study requirements
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or FDA.

What are my rights in this study?
Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

What are the costs of taking part in this study?
Your involvement in this research study is voluntary.

The research procedures only will be provided free of charge by the study sponsor while you are participating in this study. This will include the EsoCheck/EsoGuard Determination along with the upper endoscopy for qualifying EsoGuard negative subjects. A parking pass will be provided. Neither you nor your insurance provider will be responsible for the costs of any research-only tests or procedures. You and your insurance company will be responsible for payment of recommended

standard of care upper endoscopy and all other medical care that would normally be part of the treatment for Barrett's esophagus and esophagus cancer. You may wish to contact your insurance provider to determine your level of coverage prior to undergoing any non-research endoscopy procedure.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

You will not receive, either now or in the future, any compensation, royalty, or any other financial benefit, which might result from any product, procedure, or other items that may be developed from the data that is derived from such research.

If you undergo a capsule balloon test (EsoCheck) in this study you may be paid a total of $20.00 in cash or gift card for completing this one time test. You will also receive a parking voucher.

If you have a negative EsoGuard lab test and elect to undergo a research endoscopy, you may be paid an additional $60 in cash or gift card for completing the additional research test along with a parking voucher.

To receive payment you must agree to complete a W-9 form which requires you to provide an address and social security number to the accounting department. This payment to you may be considered taxable income by the IRS. You will be issued a 1099-Misc form only if payment exceeds $600 from all studies in which you are participating, in a fiscal year.

What happens if I am injured or hurt because I took part in this study?
If you believe that you are injured as a result of the research procedures being performed, please immediately contact the study doctor.

If injury occurs as a result of your involvement in this research, medical treatment is available from University Hospitals, or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions.

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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Further information about research-related injuries is available by contacting the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at [redacted].

Privacy and Confidentiality

All information gathered in this study will be linked to a unique code. You will be identified to study investigators only through this code. Study information collected from you will be stored in a locked cabinet at the institution in which you enrolled in the study.

This information will also be stored electronically in a centralized computer database. This database is located on the worldwide web. The database is password protected, and only designated study investigators and team members will have access to your information. All recommended security precautions have been taken to protect the information stored in this database.

Storage of Tissue Samples for the Purposes of this study

If you donate endoscopic tissue for this research, it will be stored indefinitely for this and future research at the Seidman Cancer Center GI Tissue Biorepository.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will contact you to let you know what they have found.

Student/Employee Rights

Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisor.

HIPAA AUTHORIZATION

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

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Amitabh Chak, MD, and the research study staff at

University Hospitals for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition.

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the University Hospitals Institutional Review Board and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- Department of Health and Human Services;
- National Cancer Institute (NCI);
- Case Comprehensive Cancer Center members and collaborators
- The Food and Drug Administration;
- The Department of Health and Human Services;
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards;
- National Institute of Diabetes and Digestive and Kidney Diseases;
- University Hospitals Cleveland Medical Center other staff from the Principal Investigator's medical practice group;
- University Hospitals, including the Center for Clinical Research and the Law Department;
- Government representatives or Federal agencies, when required by law

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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Amitabh Chak, MD
Case Comprehensive Cancer Center
University Hospitals Cleveland Medical Center
11100 Euclid Ave.
Cleveland, OH 44106

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside University Hospitals cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

University Hospitals will not use your information collected in this study for another research purpose without your written permission; unless University Hospitals Institutional Review Board assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

Voluntary Participation
Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. De-identified data from this study may be published, presented, or otherwise made publically available. If this happens, your identity will not be revealed.

The data collected on you to the point of study withdrawal will remain part of the study database and may not be removed. The study team will ask if we can continue to collect Standard of Care data from your medical record.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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Questions about the Research
If you have any questions, you can ask the Principal Investigator and/or research staff at [redacted].

Emergency or after-hours contact information
If you are a University Hospitals patient, and you need to contact study staff outside normal business hours, you may contact [redacted] and you will be transferred to the answering service, which can put you in contact with Amitabh Chak, MD or the oncologist (cancer doctor) on call.

Where Can I Get More Information?
If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about: concerns regarding the study, research participant's rights; research-related injury; or other human subjects issues, you may contact the Institutional Review Board (IRB) at the University Hospitals Cleveland Medical Center's Research Subjects Rights Phone line at [redacted].

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, if applicable, 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.

Signature
Signing below indicates that you have been informed about the research study in which you

Project Title: CASE 1221; "Detection of Barrett's Esophagus in Patients without GERD Symptoms."

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voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

_____	_____	_____
Signature of Participant	Date	Printed Name of Participant

_____	_____
Signature of Person Obtaining Consent	Date

_____
Printed Name of Person Obtaining Consent