BENAROYA RESEARCH INSTITUTE
Virginia Mason

Temporal variation in exhaled volatile organic compounds in response to therapeutic intervention in esophageal cancer patients

CONSENT TO PARTICIPATE IN A RESEARCH STUDY

IRB Number: **IRB18-101**

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SUPPORTED BY: **Salgi Foundation**

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part.

Please note the following summary regarding your study participation. A more thorough explanation is available later in this document:

- Your participation is voluntary and you may decide not to participate at any time.
- The purpose of this study is to measure molecules found in exhaled breath samples before, during, and after treatment for esophageal cancer to see if changes in the molecules can be detected.
- The procedures will include collecting your personal information and samples of your exhaled breath, urine, and saliva.
- There are at least 4 visits. Study visits will occur while you are already visiting your doctor for your normal care and will take about 20 minutes (in addition to your regular care at each visit).
- Your participation in the study will begin before you start treatment and will continue until your final visit, between six months to one year after your surgery.

- The potential risks of being in the study include temporary shortness of breath following breath sampling and loss of confidentiality of your information.
- Participating in this study is not expected to benefit you personally, but researchers hope the information gained from this study will help other people in the future.
- You will not receive any payment for participating in this study.

You are being asked to take part in this study because you have esophageal cancer and are planning on having it removed with surgery. This particular research in humans is designed by Dr. Donald Low from Virginia Mason Medical Center.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to investigate whether exhaled breath can be used to detect and monitor esophageal cancer.

Esophageal cancer ("EG cancer") affects over half a millions people worldwide every year. Early esophageal cancer typically has non-specific symptoms that are often mistaken for benign (non-cancer) conditions. As a result, patients are often referred for further investigations only when they have more prominent symptoms that are typically associated with advanced incurable disease. As a consequence, 7 out of 10 new cases of EG cancer diagnosed are considered to be at an advanced stage, with less than 1 in 3 patients eligible for potentially curative therapy. Better ways of diagnosing esophageal cancer earlier are therefore needed. An ideal test for esophageal cancer would be non-invasive, simple to administer in the community, and cost effective.

Our approach to this clinical challenge is to establish a non-invasive test for the detection of esophageal cancer that is based upon the unique signature of small molecules within exhaled breath. In this study that is being conducted in collaboration with researchers in the United Kingdom (UK), we would like to measure the levels of these small molecules within the breath of patients with esophageal cancer at different times during their treatment: (i) at diagnosis; (ii) after chemoradiotherapy, and; (iii) after surgery. By studying how the small molecules contained within the breath change as a result of esophageal cancer and its treatment, we hope to learn new information that can help develop a new test for this disease.

We will also measure the small molecules within saliva and urine samples collected at the same time as breath in order to study if there are any important differences between these three samples. We will also attempt to measure different bacteria in saliva, as this may offer clues about the origin of these small molecules within the body.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

We think about 50 people will take part in the study at Virginia Mason Medical Center.

WHAT IS INVOLVED IN THE STUDY?

Before you begin the study …

Your study doctor will review your medical records to confirm you are eligible to take part. To be eligible you must have been recently diagnosed with esophageal cancer and have not yet begun treatment, which should eventually include an operation to remove this cancer.

During the study …

If you are eligible and should you choose to take part in this study, you will need the following additional tests and assessments:

1. Breath sample: you will be asked to breathe in to a sample bag. The test is similar to blowing up a balloon, and typically takes one breath (10-20 seconds).
2. Urine sample: you will be asked to provide a urine sample.
3. Saliva sample: you will be asked to provide a saliva (spit) sample.

Each of these tests and assessments are designed to accurately measure your nutritional status (the level of nutrients in the body, and how the body uses them) and will be performed on four separate occasions:

1. Before you begin chemotherapy or chemoradiotherapy, at your routine hospital visit*.
2. After you finish chemotherapy/chemoradiotherapy, but before your surgery to remove the cancer.
3. After your surgery.
4. At the time of your routine postoperative follow-up (6-12 months after your surgery).

   **If you attend the hospital on more than one day, you may be asked to give a second breath sample to look at the short term variation in the levels of breath molecules.*

At your first visit, you will also be asked to fill out a one page survey about giving a breath sample.

We have chosen to perform these additional tests and assessments on a day when you will be attending the hospital to undergo either a surgery or endoscopy as part of your routine care. As a result you will have been asked by your doctor not to have eaten anything on the day of your visit in preparation for this routine surgery or endoscopy. Taking part in this study will not require you to fast for any longer than is planned for your routine care. The study doctor will ask you to provide information about what food and drinks you have consumed prior to your visit to the hospital. You will also be asked about your smoking habits and any exercise you may have recently undertaken.

However, it is possible that even after consenting and evaluation, some participants may not be eligible for treatment. It is important to know your samples during study visits are valuable to this study for comparison purposes.

HOW LONG WILL I BE IN THE STUDY?

There will be four study visits that will take around 20 minutes to complete all of the tests and assessments outlined above.

You can stop participating in the study at any time. If you decide to stop being in the study, please talk to the researcher and your regular doctor. A decision not to take part or to withdraw

from this study will not affect the standard of care you receive. If you do decide to end your participation, any samples that have been collected from you will be kept and used for the study purposes described in this form, then will be destroyed immediately after testing.

WHAT ARE THE RISKS OF THE STUDY?

Risks and side effects related to the study procedures may include:

Less Likely:

- Temporary shortness of breath following breath sampling.

For more information about risks and side effects, ask the researcher or contact Dr. Donald Low at (206) 223-6164.

There is also a risk of loss of confidentiality of your information. You will read about the steps taken to protect your information later on in the firm.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there will not be any direct benefit to you. We hope to use the results of this study to improve the care and quality of life of other patients in the future.

In the unlikely event the analysis of your samples or measurements produces information directly relevant to you or your treatment, we will communicate this to the team in charge of your care.

WHAT OTHER OPTIONS ARE THERE?

You may choose not to participate in this study. If you choose not to take part in this study, you will continue to receive your standard care.

WHAT ARE THE COSTS?

This study has been fully funded by the Salgi Foundation. Taking part in this study will not lead to any additional costs to you or your insurance company.

You will receive no payment for taking part in this study.

WHAT IF YOU GET INJURED BECAUSE YOU TOOK PART IN THIS STUDY?

It is important that you tell your study doctor, Dr. Donald Low, if you feel you have been injured because of taking part in this study. Tell your doctor in person or call him at (206) 223-6164.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. No funds have been set aside to

compensate you in the event of injury. This does not limit your ability to seek compensation for study related injuries.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary, and you may choose not to take part or may leave the study at any time. Choosing not to take part or leaving the study will not result in any penalty or loss of benefits to which you are entitled outside of this research.

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

- You may contact your doctor for any questions about your care.
- For questions about study procedures, study costs, or to report a study-related injury, contact the researchers Dr. Donald Low or Dr. Piers Boshier at (206) 223-6164.
- For questions about your rights as a research participant, contact the BRI Institutional Review Board (IRB) Manager at (206) 342-6916. The IRB Administrator manages the IRB, which is a group of people who review this research to protect your rights and welfare.

WHERE CAN I GET MORE INFORMATION?

You will get a copy of this consent form. You may also request a copy of the protocol (full study plan) by contacting Dr. Donald Low at (206) 223-6164.

HOW WILL MY IDENTIFIABLE INFORMATION AND BIOLOGICAL SAMPLES BE USED?

The samples you provide in this study will be used for the purposes described in this form only. Your samples will not be used or distributed for future research studies even if identifiers are removed. It is possible, however, that your biological samples may be used for commercial profit. There are no plans to provide financial compensation to you.

We will store your information gathered as part of this study to use for future research. We have an established research database that stores data from thoracic surgery studies like this one, so researchers can perform additional research and quality improvement projects using information gathered from previous studies. It is intended that this database will help to support a better understanding of some of the challenges faced by both patients and clinicians in the field of esophageal surgery. Specifically we hope to better understand factors that affect patient's response to treatment and/or long-term outcomes. Such evidence will ultimately help clinicians in the role of supporting patients as they make decisions in relation to their care.

For future research with your information, researchers might remove identifiers (such as your name and date of birth), and the de-identified information might be used or shared with other researchers for future research without any additional consent from you. Findings or results from any future research would not be reported back to you.

AUTHORIZATION TO USE AND/OR DISCLOSE PROTECTED HEALTH INFORMATION FOR RESEARCH

We are required by special federal and state privacy laws to protect the privacy of your health information under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule. Researchers (investigators) would like to use your health information for research. This section describes what researchers will do with information about you. To learn more about your individual privacy rights, you may ask your provider for a Notice of Privacy Practices.

WHAT IS PROTECTED HEALTH INFORMATION (PHI)?

PHI is information gathered by a health care provider, health plan, or researcher that identifies you or which includes information that may tie your identity to your health record.
PHI includes:

- Information from your existing or future medical records needed for this study as described in this form; and/or
- Information about you created during this study, as described above.
- This health information generally includes: demographics information, result of physical exams, histories and physicals, X-rays, diaries, questionnaires, records of treatments and side effects of treatments, and in regard to this study also includes: the results of breath, urine, and saliva testing.

WHO MAY USE OR SHARE MY PHI?

Virginia Mason and its health care providers, including but not limited to its primary care providers, are permitted to disclose your PHI to the Principal Investigator and Sub-Investigators (collectively, “Researchers”) listed in the Consent. The Researchers may also use and disclose your health information between each other and with the other individuals and entities listed in this Authorization.

WHAT MAY THE RESEARCHERS DO WITH MY PHI?

The researchers will use your health information to conduct the research. As part of the research they may share your information with certain people and groups. These may include:

- The sponsor of this study, Dr. Donald Low, at Virginia Mason Medical Center Department of Thoracic Surgery & Thoracic Oncology. The sponsor reviews the study and researchers must share some information with the sponsor.

- The Institutional Review Board (IRB) that approved this research, Benaroya Research Institute (BRI) IRB. The IRB reviews, audits, and monitors studies to protect the rights and safety of research participants.
- BRI Regulatory Compliance and Education Department will conduct routine internal quality reviews audits and monitor visits of the study and patient records.
- BRI coordinators, managers and assistants for the purposes of research study administrative and related support, including but not limited to pre-screening and follow up for research participants, and reporting to sponsors and government agencies.
- Federal and state agencies and their representatives that have oversight of the research study or to whom access is required under the law, which include but are not limited to:
    - Food and Drug Administration
    - Office for Human Research Protections
    - National Institutes of Health
- Your health insurer(s) if they are paying for care provided as part of the research.

HOW WILL MY HEALTH INFORMATION BE KEPT PRIVATE?

All efforts will be made to keep your personal information confidential; however, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

Researchers will remove your name (and other information that could identify you) from your study information before sharing it with any individual outside of the local research team. Your study information and samples will be labeled with a code. If research findings are published from this study, they will not identify you unless you allow it in writing.

WHAT HAPPENS IF I WANT TO WITHDRAW MY AUTHORIZATION?

You may change your mind at any time and withdraw this authorization. This request must be made in writing to the investigator Dr. Donald Low, at the address listed on page 1 of this form. Beginning on the date you withdraw, no new identifiable health information will be used for research. However, the researchers may continue to use and share the information that was provided before you withdrew your permission. If you withdraw your authorization, you will not be allowed to continue in this research study.

HOW LONG WILL THIS AUTHORIZATION LAST?

If you agree by signing this form, the researchers can use and share your identifiable health information for the next 50 years. If you do not want to provide the researchers with permission to use and share your information, you should not sign this form, and will not be able to participate in this research. The authorization will expire 50 years from the date you sign it, unless you withdraw your permission as directed above. The 50 year period is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be completed.

PARTICIPANT'S CONSENT AND AUTHORIZATION

I have read and been given a chance to ask questions about this consent form and HIPAA authorization. I agree to take part in this study and agree to the use and sharing of my information as described in this form. I will receive a signed copy of this consent form and HIPAA authorization.

PARTICIPANT'S SIGNATURE	**PARTICIPANT'S NAME** (print)	**DATE**

CERTIFICATE OF PERSON OBTAINING CONSENT:

I have provided an explanation of the above research study, and have encouraged the subject to ask questions and request additional information regarding the study and possible alternatives. A copy of this consent form has been given to the subject.

SIGNATURE OF PERSON OBTAINING CONSENT	**NAME OF PERSON OBTAINING CONSENT** (print)	**DATE**

WITNESS STATEMENT (if needed)

As an impartial third party, I witnessed the entire consent discussion and the participant's signature on this form.
This person had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

Name of Witness *(Print)*

Signature of Witness	**Date**