Clinical Research Unit
Tom Baker Cancer Centre
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Calgary
T2N 4N2

Informed Consent Form for Participation in a Research Study

Concordance of Molecular Classification Based on Fine Needle Biopsy (FNB) and Surgical Samples

Molecular Risk by FNB

Protocol ID: HREBA.CC-23-0001

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Sponsor/Funder(s): Qualisure Diagnostics, Inc

You are being invited to participate in a research study because you have a fine needle biopsy (FNB) that shows that you have a high likelihood of having papillary thyroid cancer (PTC) and are eligible for partial or total thyroidectomy.This consent form provides detailed information about the study to assist you with making an informed decision. Please read this document carefully and ask any questions you may have. All questions should be answered to your satisfaction before you decide whether to participate.

The study staff will tell you about timelines for making your decision. You may find it helpful to discuss the study with family and friends so that you can make the best possible decision within the given timelines.

Taking part in this study is voluntary. You may choose not to take part or, if you choose to participate, you may leave the study at any time without giving a reason. Deciding not to take part or deciding to leave the study will not result in any penalty or any loss of medical or health-related benefits to which you are entitled.

On behalf of the study doctor, who is one of the researchers, a member of the study team will discuss this study with you and will answer any questions you may have. If you do consent to

participate in this study, you will need to sign and date this consent form. You will receive a copy of the signed form.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Thyroid cancer is the 8th most common cancer, and incidence has been increasing. PTC accounts for most thyroid cancers. Treatment decisions related to PTC depend on the doctor's estimate on whether the cancer is aggressive or not. Current methods for distinguishing aggressive tumors from less aggressive tumors rely on clinical factors as well as factors related to the final pathology (after the tumor has been removed). Ideally, the information required to make decisions would be available prior to surgery, so that surgical decisions can be made.

A new test is being developed to determine molecular features of a PTC and to estimate the risk of cancer recurrence after surgery. Thyroid GuidePx® provides unique information that may inform doctors' decisions. The greatest potential for Thyroid GuidePx® to impact on clinical care is if it can be performed prior to surgery on a fine needle biopsy (FNB). If Thyroid GuidePx® could be done on an FNB, it would inform surgeons on the type of surgery that would be most appropriate for an individual.

Health Canada, the regulatory body that oversees the use of natural health products, drugs and devices in Canada, has not approved the sale or use of this test to treat this kind of cancer. However, the test when performed on surgical samples is available for sale in the United States.

The Health Research Ethics Board of Alberta – Cancer Committee (HREBA-CC), which oversees the ethical acceptability of research involving humans, has reviewed and granted ethics approval for this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine whether results from a fine needle biopsy are the same as results from a larger sample that is acquired from the surgical pathology.

WHAT ARE OTHER OPTIONS IF I DECIDE NOT TO PARTICIPATE IN THIS STUDY?

You do not have to take part in this study, in order to receive continued medical care. If you decide not to participate in the study, then your surgeon and your care doctor will provide you with the standard care for any patient like you with PTC.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

We plan to enroll ~130 people at the Foothills Medical Centre (Alberta Health Services) and at the University of Calgary Medical Clinic.

WHAT WILL HAPPEN DURING THIS STUDY?

STUDY PROCEDURES

Following consent, you will undergo surgery as planned by your surgeon. Participating in the study will have no influence on your surgery or treatment. We will collect clinical and pathological information related to you. The schedule for follow-up after surgery will be determined by your surgeon and other care doctors. Researchers will be informed whether your cancer has returned after surgery.

MANDATORY SAMPLE COLLECTION

The researchers doing this study need to do tests on samples as described below. The collection of these samples is a necessary part of this study and will be used only for this purpose. Hereditary genetic testing (to look at whether cancer runs in your family) will not be done on these samples. The samples will not be sold. Reports about research tests done with your samples will be given to the study doctor(s). If you would like to learn the results of this research, please let them know.

Tissue Collection

As part of this study, you will need to have a fine needle biopsy. During surgery, while you are asleep, your surgeon will take a small amount of tissue or fluid from your tumor using a very thin needle and syringe once the tumor is clearly visible to the surgeon. The cellular material from the fine needle biopsy will be sent to the central laboratory for processing.
Separate surgical samples will be processed and examined in the usual fashion by the Pathology Department, Alberta Precision Laboratories, Calgary, AB, Canada. This process will follow routine specimen processing protocols and will not interfere with standard methods of pathologic diagnosis. If there is any remaining tissue available, we would also take a leftover sample of your tumor after all diagnostic tests have been performed. Tissue will be released for research only once sufficient tissue is taken for diagnostic and clinical use

Experimental Procedures

The following test is considered experimental and will only be done for participants on this study:

- Thyroid GuidePx®: This diagnostic test will be performed in a sample taken by fine needle biopsy during surgery, and the test will also be performed on the surgical sample. The test results will be compared in the fine needle biopsy and the (larger) surgical sample to determine how closely the results resemble each other. The technicians performing the test will be blinded, which means that they will not know what fine needle biopsy matches each surgical sample. In addition to comparing Thyroid GuidePx® results using the two methods of collecting sample, the researchers will follow participants over time to obtain more information on the capability of the test to estimate the risk of the cancer recurring after surgery.

The Thyroid GuidePx® test will be performed at OncoHelix, a clinical laboratory with expertise in precision oncology located at the Cumming School of Medicine, University of Calgary, or at Protean BioDiagnostics, a clinical laboratory with expertise in Precision Oncology in Orlando, FL. The location of the testing will depend on how soon testing can be performed at each laboratory.

Once the test have been completed, any leftover samples will be returned to the facility from which they were obtained if needed, or destroyed, unless you wish to give permission for other future research purposes, in which case you will be given a separate optional consent form to sign.

Identification of Samples

To protect your identity, the information that will be on your samples will be limited to the unique study code that will be assigned to you, the date of the procedure, and the type of sample collected. The clinical laboratory performing Thyroid GuidePx® will receive information related to your surgery as they will provide the full report of the results of the test on the surgical specimen

for you and your doctor to review.
Despite protections being in place, there is a risk of unintentional release of information that could lead to loss of privacy. Due to technological advances in genetics, there is also a risk of unintentional release of genetic information from the samples. This information can be linked back to you and can lead to possible future discrimination in employment or insurance, against you or your biological relatives.

Withdrawal of Samples

If you no longer want your samples to be used in this research, you should tell the study doctor. If possible, they will have the samples returned to the hospital from which they were obtained (if needed), or destroyed. However, if your samples have already been sent to researchers, it will not be possible to recall them and their associated data.

If tests have already been done on your sample(s) it will not be possible to withdraw those results. However, no further testing will be done.

OPTIONAL RESEARCH

The researchers doing this study are interested in doing additional optional research. You will be given a separate optional study consent form(s) to read and sign if you wish to give permission for this. You may decide not to participate in the "optional" study and still participate in this main study.

WHAT ARE THE POTENTIAL SIDE EFFECTS FROM PARTICIPATING IN THIS STUDY?
With tissue removal related to fine needle biopsy, there may be a slightly increased risk of bleeding or injury to neighbouring organs (less than 1%), but that risk is small in comparison to the planned surgical procedure. The risks of the standard or usual treatment will be explained to you as part of your standard care. These risks are not included in this consent form.

Thyroid GuidePx® provides an estimate of the likelihood of recurrence within 5 years, based on our studies so far. Recurrences can appear after 5 years. There are risks to making clinical decisions based on diagnostic tests such as Thyroid GuidePx®. Specifically, if a tumor is reported as “Low Risk”, then it is possible that a tumor could be undertreated because of clinical decisions stemming from that test result. Additionally, if a tumor is reported as “High Risk”, then it is possible that a tumor could be overtreated because of clinical decisions stemming from that test result.

The Thyroid GuidePx® test has not yet been approved by Health Canada. Therefore, while it may add information to help with understanding the risk of the cancer coming back after surgery, it is considered “experimental.” Although preliminary data are promising, it is NOT proven that results will be better than standard of care.

Thyroid GuidePx® does *not* yield information on other diseases, and it does *not* reveal information on paternity if more than one family member is tested.

A Data and Safety Monitoring Board (DSMB), an independent group of experts, will be reviewing the data throughout the conduct of the study to ensure continuing participant safety as well as scientific validity and quality of the research. A clinical research organization, Lumiio, will be responsible for forming the DSMB.

WHAT ARE THE REPRODUCTIVE RISKS?

This study will not affect reproduction, the ability to breast feed, or fetal development.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

Participation in this study may or may not be of personal benefit to you. The results of the Thyroid GuidePx® test may provide additional information related to the risk of cancer recurrence after surgery but there is no guarantee that the intervention may be of direct benefit to you. However, based on the results of this study, it is hoped that in the long-term, patient care can be improved.

WHAT ARE MY RESPONSIBILITIES AS A STUDY PARTICIPANT?

If you choose to participate in this study, you will be expected to:

- Permit the collection of a fine needle biopsy and surgical sample from the tumor site
- Permit the use of clinical information from your medical charts and reports

WILL THERE BE ANY LONG-TERM FOLLOW-UP INVOLVED WITH THIS STUDY?

In the event that it is necessary to further evaluate the efficacy of the Thyroid GuidePx®, it may be necessary to have access to additional information about your health status. The study team may attempt to obtain study-related information about your health from you or from other private sources, including your care physician. This may include contacting you again by phone or letter, but only if you have not withdrawn your consent for future contact. However, contacting you, your care physician or using other private sources of information, is optional. Please indicate your decision using the check boxes below.

You give permission to the study doctor or member of the study team to attempt to obtain study-related information about your health status to further evaluate the safety or efficacy of the Thyroid GuidePx®.This may include contacting your care physician, or by contacting you by phone or letter (i.e., future contact).

☐ Yes ☐ No Participant's Initials: _____

Name/phone number of care physician: _____

In addition, the study team may also attempt to obtain study-relevant information about your health information from public sources such as national patient registries (e.g., cancer registries).

CAN I CHOOSE TO LEAVE THIS STUDY EARLY?

You can choose to end your participation in this research (called early withdrawal) at any time without having to provide a reason. If you choose to withdraw early from the study, you are encouraged to contact the study doctor or study staff. You may withdraw your permission to use information that was collected about you for this study at any time by letting the study doctor know. However, this would also mean that you withdraw from the study.

Information that was recorded before you withdrew will be used by the researchers for the purposes of the study, but no additional information will be collected or sent to the sponsor after

you withdraw your permission.

CAN MY PARTICIPATION IN THIS STUDY END EARLY?

Some of the patients who consent to the study will find out after surgery that they do not have PTC. In those patients, the Thyroid GuidePx® test will not be performed, no further data collection will be needed.

HOW WILL MY PERSONAL INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate, the researcher and study staff will only collect information they need for this study. This will include personal health information such as your age, sex, any additional health concerns, and information related to the pathology details of your tumor.

Studies involving humans sometimes require collection of information on race and ethnicity as well as other characteristics of individuals because these characteristics may influence how people respond to different interventions. Providing information on your race or ethnic origin is voluntary.

Records identifying you, including information collected from your medical files/records, such as your Electronic Medical Records (EMR), Netcare, charts, etc., will be kept confidential to the extent permitted by the applicable laws, will not be disclosed or made publicly available, except as described in this consent document.

The researcher and study staff will do everything that they can to make sure that this information is kept private and confidential. Samples stored at the University of Calgary and shipped to off-site locations for analysis will be de-identified and assigned a study code. Only the study team at the University of Calgary will be able to use the study code to identify you in the event you ask for your samples to be destroyed.

Authorized representatives of the following organizations may look at your identifiable medical/clinical study records at the site where these records are held for quality assurance purposes and/or to verify that the information collected for the study is correct and follows proper laws and guidelines:

- Members of the Regulatory/Audit team at University of Calgary for quality assurance purposes
- The Health Research Ethics Board of Alberta – Cancer Committee, which oversees the ethical conduct of this study
- Health Canada, which oversees the use of natural health products/drugs/devices in Canada and the conduct of clinical trials
- Other regulatory agencies that have oversight of this study

Authorized representatives may **receive** information related to the study from your medical/clinical study records that will be kept confidential in a secure location and may be used in current or future relevant health research. Your name or other information that may identify you will not be provided (e.g., the information will be de-identified). The records received by these organizations will be coded with a number. The key that indicates what number you have been assigned will be kept secure by the researchers directly involved with your study and will not be released.

The following organizations may receive study data:

- Qualisure Diagnostics, Inc., Calgary, Alberta (https://qualisuredx.com)
- OncoHelix, Calgary, Alberta (https://oncohelix.org)
- Protean BioDiagnostics, Orlando, FL (https://www.proteanbiodx.com/)
- Lumiio (https://www.lumiio.com)

To protect your identity, the information that will be on your specimen will be limited to your study code, date of sample collection, and type of sample collected. Any disclosure of your identifiable health information will be done in accordance with federal and provincial laws including the Alberta Health Information Act (HIA). The organizations listed above are required to have organizational policies and procedures to protect the information they see or receive about you, except where disclosure may be required by law. The study doctor will ensure that any personal health information collected for this study is kept in a secure and confidential location at the University of Calgary as also required by law.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during the study will be used in analyses and will be published/presented to the scientific community at meetings and in journals. This information may also be used as part of a submission to regulatory authorities around the world to support the approval of this intervention.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated. Every effort will be made to keep your identifiable information confidential, and to follow the ethical and legal rules about collecting, using and disclosing this information.

Any study-related information and samples if applicable sent outside of Canadian borders may increase the risk of disclosure of information because the laws in those countries dealing with protection of information may not be as strict as in Canada. However, all study data and samples that is transferred outside of Canada will be coded (this means it will not contain your personal identifying information such as your name, address, medical health number or contact information). Any information will be transferred in compliance with all relevant Canadian privacy laws. By signing this consent form, you are consenting to the disclosure of your coded information to organizations located outside of Canada.

A copy of the consent form that you sign to enter this study will be included in your medical record/hospital chart. Study records will be kept separate from your medical records. After the study is done, we will still need to securely store your data that was collected as part of the study. We will keep your data and study records stored for 25 years after the end of the study.

WILL MY HEALTHCARE PROVIDER(S) BE INFORMED OF MY PARTICIPATION IN THIS STUDY?

Your family doctor/health care provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know, if you like. If you are undecided, the study doctor can discuss this with you.

WILL THERE BE ANY COSTS INVOLVED WITH PARTICIPATING IN THIS STUDY?

The Thyroid GuidePx® test will be given to you free of charge while you take part in this study.

WILL I BE COMPENSATED FOR PARTICIPATING IN THIS STUDY?

You will not be paid for taking part in this study. Your tissue will be used for research purposes only. It is possible that the research conducted using your samples and/or study data may eventually lead to the development of a new diagnostic test. There are no plans to provide payment to you if this happens. Samples collected will strictly be utilized for cancer research, but may also have commercial end uses such as for the purpose of diagnostic tests.

In the case of research-related side effects or injury, medical care will be provided by your doctor or you will be referred for appropriate medical care. Although no funds have been set aside to compensate you in the event of injury or illness related to the study procedures, you do not give up any of your legal rights for compensation by signing this form. This consent form does not relieve the researcher(s), the hospital, the sponsor, and their agents from their legal and professional responsibilities.

WHAT ARE MY RIGHTS AS A PARTICIPANT IN THIS STUDY?

You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.You have the right to be informed of the results of this study once the entire study is complete. If you would like to be informed of these results, please contact the study doctor.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the hospital, investigators, sponsor, involved institutions for compensation or their agents, nor does this form relieve these parties from their legal and professional responsibilities.

IS THERE CONFLICT OF INTEREST RELATED TO THIS STUDY?

The principal investigator, Dr. Oliver Bathe, is the founder and CEO of Qualisure Diagnostics, Inc. Dr. Adrian Harvey is an advisor to Qualisure Diagnostics, Inc. Dr. Karen Kopciuk is a shareholder of Qualisure Diagnostics, Inc. Dr. Cynthia Stretch is a co-founder and Chief Scientific Officer of Qualisure Diagnostics. Dr. Faisal Khan is a co-founder and director of OncoHelix. Dr. Anthony Magliocco is the founder and CEO of Protean BioDiagnostics.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT ME AS A RESEARCH PARTICIPANT?

During the study, the researchers may learn something about you that they didn't expect. For example, the researchers may find out that you have another medical condition. If any clinically important information about your health is obtained as a result of your participation in this study, you will be given the opportunity at that time to decide whether you wish to be made aware of that information.

WHERE CAN I FIND ONLINE INFORMATION ABOUT THIS STUDY?

A description of this clinical trial will be available on http://www.clinicaltrials.gov. This website will not include information that can identify you. You can search for this website at any time.

WHO DO I CONTACT FOR QUESTIONS?

If you have questions about taking part in this study, you should talk to the researcher, co-investigator or study coordinator. These person(s) are:

Dr. Caitlin Yeo	403-944-0966
Name	Telephone
Elleine Allapitan	403-220-8440
Name	Telephone

If you have questions about your rights as a participant or about ethical issues related to this study and you would like to talk to someone who is not involved in the conduct of the study, please contact the Office of the Health Research Ethics Board of Alberta – Cancer Committee at:
Telephone: 780-423-5727 Toll Free: 1-877-423-5727

SIGNATURES

Part 1 - to be completed by the potential participant.

	Yes	No
Do you understand that you have been asked to take part in a research study?	☐	☐
Do you understand why this study is being done?	☐	☐
Do you understand the potential benefits of taking part in this study?	☐	☐
Do you understand the risks of taking part in this study and the risks of becoming pregnant or fathering a child during this study?	☐	☐
Do you understand what you will be asked to do should you decide to take part in this study?	☐	☐
Do you understand the alternatives to participating in this study?	☐	☐
Do you understand that you are free to leave the study at any time, without having to give reason and without affecting your future health care?	☐	☐
Do you understand who will see your records, including health information that identifies you?	☐	☐
Do you understand that by signing this consent form you are giving us permission to access your health information and specimens if applicable?	☐	☐
Do you understand that by signing this consent form that you do not give up any of your legal rights?	☐	☐
Do you understand that your family doctor/health care provider will/may be informed of your participation in this study?	☐	☐
Have you had enough opportunity to ask questions and discuss this study?	☐	☐

By signing this form I agree to participate in this study and I understand that the research team will have access to my individually identifying health information for research purposes. In cases where the study involves an intervention such as a research-related medication, device, or other therapy, or the project includes research-specific lab tests and/or imaging, your signed consent will also be included in your electronic medical record(s), and healthcare staff will know that you are in a research study.

Signature of Participant	PRINTED NAME	Date

Part 2 - to be completed by the study doctor or designee who conducted the informed consent discussion. Only compete this section if the potential participant has **agreed** to participate.

I believe that the person signing this form understands what is involved in the study and has freely decided to participate.

Signature of Person Conducting the Consent Discussion	PRINTED NAME	Date

Part 3 - to be completed only if the participant is unable to read or requires assistance of an oral translator/interpreter.

- The informed consent form was accurately explained to, and apparently understood by the participant.
- Informed consent was freely given the participant.

Signature of Impartial Witness/Interpreter	PRINTED NAME	Date

You will be given a copy of this signed and dated consent form prior to participating in this study.