

Participant Information and Consent Form

Early Detection of Lung Cancer – A Pan-Canadian Study

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Sponsor: Terry Fox Research Institute

Emergency Contact Number (24 hours / 7 days a week): 604-875-5000

Non-Emergency contact numbers are noted at the end of this document under the section heading “Who Do I Call if I Have Questions or Concerns”.

This is a longitudinal research study (study of a group of people over time). Research studies include only individuals who choose to take part. Please take your time to make your decision. Discuss it with your friends and family. This form will tell you what you need to know about this study. If you agree to take part in this study, you need to sign this form. Your signature means that you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study. Your participation is voluntary. You can stop participating at any time and withdraw from the study and you will continue to be offered the best available medical care.

EARLY DETECTION OF LUNG CANCER

Lung cancer is the most common cause of cancer death in Canada. At the present time, only 16% of lung cancer patients survive 5 years or more because the majority of the patients are diagnosed too late when they present with symptoms. If lung cancer is diagnosed early (through screening) and treated early before it spreads outside the air passages, over 77% of patients survive 5 years or more. Early detection and treatment of lung cancer is a promising way to reduce lung cancer deaths. Previous efforts at screening have not been successful in decreasing the death rate from lung cancer because the screening tests that were available were either not sensitive enough to pick up small cancers (by chest x-ray) or detect very few cancers (by sputum cytology, which means examining a person's lung phlegm (mucous) for cancer cells).

New technologies such as spiral computed tomography, often just called “CT scan” and autofluorescence bronchoscopy can pick out tiny cancers that are not visible by previous tests. In an autofluorescence bronchoscopy a blue light instead of a white light is used in the camera. However, these newer tests are more expensive. CT scan also picks up abnormal areas that are not related to lung cancer leading to unnecessary additional tests or treatment that are of no benefit and may even be harmful to those who take part in the screening. To predict lung cancer risk more accurately so that only those with significant

risk of lung cancer will be screened, we have developed a risk prediction tool based on age, smoking history, occupational exposure, a family history of lung cancer, educational level and body mass index (height and body weight).

Why Is This Study Being Done?

This study may help identify optimal ways of detecting early stage lung cancer. We hope that the risk prediction tool combined with improved methods of identifying the early cancer may help lead to ways in which the number of lung cancer deaths can be reduced. The general aim of this study is to find out how to best screen for lung cancer using the latest available methods such as CT scan and autofluorescence bronchoscopy. The specific goals are

1. to determine if we can improve the accuracy of the risk prediction tool further, by adding a simple breathing test called spirometry and/or a blood test.
2. to see what combination of tests (including CT scan and autofluorescence bronchoscopy, spirometry, and blood test) is the most accurate for detecting early lung cancers.
3. to find out how the screening tests, follow-up visits to doctors, additional tests or treatment may affect the quality of your life, such as your anxiety level.
4. to determine the actual costs related to the screening program, such as other diagnostic tests and treatment and the use of health care resources. This will allow us to calculate how much it would cost the public if a lung cancer screening program were to be carried out in Canada.

This research study is being conducted across Canada. In British Columbia, the study will be conducted under the supervision of Dr. Stephen Lam & Dr. Annette McWilliams at the BC Cancer Agency – Vancouver Center. The study is sponsored by the Terry Fox Research Institute and the Canadian Partnership Against Cancer.

How Many People Will Take Part in the Study?

2,500 people will take part in this multi-center study – about 400 people will be recruited in British Columbia.

You May Participate in This Study If You:

- Are between the 50 and 75 years of age
- Have smoked cigarettes for 30 years or more
- Have a 2% or greater chance to develop lung cancer in the next three years from the risk prediction tool which asks questions about your smoking history, age, education level, family history, etc.

You Should Not Participate in This Study If You:

- Have been diagnosed with lung cancer before.
- Have had other cancer before except for non-melanomatous skin cancer, localized prostate cancer, carcinoma in situ (CIS is an early stage cancer) of the cervix, or superficial bladder cancer with your last treatment more than 6 months before registration into this study.
- Are currently taking any anticoagulants or blood thinners such as coumadin or heparin
- Are using any home oxygen (continuous or intermittent use)
- Have other serious illnesses that are not well controlled, such as infection, heart problems or stroke
- Have a known reaction to Xylocaine, Salbutamol, Midazolam, and Alfentanil
- Are pregnant.
- Have quit smoking for more than 15 years
- Have had a chest CT scan within the last 2 years

Study Procedures

Before being registered on the study:

You will be asked to answer a short screening questionnaire regarding your age, smoking history, occupational exposure to substances that are known to cause lung cancer, a family history of lung cancer, educational level and your height and weight. This is to estimate your risk of developing lung cancer over the next three years. If your 3-year lung cancer risk is equal to or greater than 2% from our prediction tool, and you are interested in the study, you will be asked to sign this consent form.

After registering (or joining) the study:

You will be asked to fill out three questionnaires, give a sample of blood (about 3 tablespoons or 45cc) and have a simple breathing test. One questionnaire is to ask about your lung cancer risk factors, past medical problems, symptoms, history of lung cancer in your immediate family and medications you are taking. The second questionnaire is to ask you about the general well being (quality of life). The third questionnaire is to ask you about your anxiety level taking part in the screening study. The blood sample will be used to measure proteins, DNA and other substances that may predict or be related to the presence of lung cancer. On a separate day a CT scan of your chest will be done. The first 50% of the participants will also receive a standard white light and autofluorescence (blue light) bronchoscopy. The second 50% of participants will not have a bronchoscopy. Your study doctor will tell you if you are one of the first 50% of participants.

These tests (CT and/or bronchoscopy) may be normal or may show an abnormality which may or may not look like cancer. If the tests are normal, then you will be followed up every 6 months for 2 years by telephone or an in-person interview to find out if you have had other tests or treatment for lung cancer. The quality of life and anxiety state questionnaires will be repeated 1 month after you have received a letter from us by mail informing you the results of your CT scan and bronchoscopy. Blood samples for measurement of proteins (about 2 tablespoonfuls or 30 cc) will be taken yearly for two years.

If either of the tests show an abnormality, the appropriate additional tests and follow-up will be added to the every 6 months telephone or in-person interview, and blood work described above. In addition, you

will be asked to answer the quality of life and “anxiety state” questionnaires again 1 month after any additional follow-up CT scans. Possible abnormal findings from these tests are described below. If you would like to meet with the study coordinator or physician to discuss the results, you can call Dr. Lam or Dr. McWilliams’ office to make an appointment using the number listed below

You will also be asked if you want to participate in a separate research study where your blood and tissue will be stored for future research. This will be explained in more detail in a separate document. If you wish to take part in this additional study, no additional blood sample is necessary, but the blood already obtained will be kept for future studies related to screening or cancer related research. You may still participate in this lung cancer screening study even if you do not wish to allow your blood and tissue to be stored for future research.

If you currently smoke, you will receive advice regarding smoking cessation to reduce the risk of lung cancer and other smoking related diseases. If you have stopped smoking, a urine sample will be taken to confirm lack of exposure to tobacco smoke as it may influence the interpretation of the results of the study.

You will be asked to fill out a monthly planner diary (which we will provide) with any tests or treatment you may have. If you are going to be admitted to hospital for test or treatment of lung cancer, we ask that you notify our study coordinator. If you will have surgery for lung cancer, a blood sample (about 2 tablespoonfuls or 30 cc) will be taken for this study before your surgery and 3 to 6 months after treatment of your lung cancer. The proteins/substances or the DNA will be measured in the blood samples taken before and after your treatment and compared to see if there is a difference.

Six and eighteen months after you begin the study, you will be contacted by phone. At this time we will review if you have undergone additional test or treatment for lung cancer. Once a year for two years (months 12 and 24 after you begin your study), you will be asked to return. The quality of life and anxiety state questionnaires will be repeated. A blood sample and breathing test will be taken for this research purposes.

Explanation of Study Tests

Low Dose Spiral Computed Tomography (CT) of the Chest

In a normal chest x-ray, a back to front and side to side view of your lungs is taken. Small nodules (or shadows), which may be indicative of early lung cancer, are difficult to see. Spiral CT makes very detailed pictures of the lungs and nodules as small as 1 mm (millimeter) can be seen. You will be asked to take a deep breath and hold it for 20 seconds, if you are able, during the scanning procedure. A CT scan takes about 15 minutes.

Bronchoscopy

The first 1,250 participants across Canada will have a bronchoscopy.

The lungs are made up of bronchial tubes or air passages. These are hollow “tubes” (bronchi) that branch off from your windpipe (trachea). Bronchoscopy is a common procedure which uses a camera scope to look into your airways after giving you a local freezing and some medicine through an IV (a needle into a

vein) that will help you relax . The purpose of this test is to see if it can find early lung cancers that are missed on CT scan.

On the day of the bronchoscopy, you will be asked to report to the clinic one hour before the time of the examination. You should not eat or drink for at least 6 hours before the examination. A small tube with a needle on the end called an IV will be inserted into a vein in your arm to give you fluids and medications during the procedure. Before and during the procedure, you will be given a mild sedative (Midazolam) to help you relax. A drug will also be given during the procedure to prevent coughing. This drug, called Alfentanil, may make you sleepy but this effect will wear off soon after the procedure is done. A local anesthetic, or freezing (Lidocaine) will be sprayed to the back of your throat to stop the gagging sensation during the procedure.

The bronchoscopy will be done using a scope the size of a pencil with a video camera that is inside the tip of the scope. The video camera is used to show and record pictures of the bronchial tubes. During fluorescence examination, instead of an ordinary white light, a blue light is used. Under the blue light, normal tissue appears green while pre-cancerous or cancerous areas appear brownish red or red.

The bronchoscopy will take about 30 minutes. You will be asked to arrive one hour prior to the procedure. You will be asked to stay for one hour after the bronchoscopy, until the effect of the local freezing in your mouth has worn off and you are not drowsy from the mild sedative. You will require another adult to escort you home. You will not be allowed to drive home on your own even though you may feel fully awake.

A small (1-2 mm) tissue sample or biopsy will be taken in any area that your doctor thinks may be cancerous. The tissue sample will be looked at by a pathologist.

Cells from your airways will also be collected by rinsing the lining your bronchial tubes with sterile sea water and a little brush will be used to collect cells.. The cells will be looked at under a microscope to see if there are any cancer cells.

What Happens Next?

If a lung cancer is found, you will be referred back to your family physician, surgeon, or respiratory medicine specialist for recommendation regarding treatment. A variety of treatments are currently available especially for lung cancers that are discovered early.

If you do not have any abnormality on your first CT scan, you will be asked to have a repeat scan at 12 months to find out if any new abnormality develops in the interval.

If you have an abnormality on your first CT scan, you will be informed by telephone and we will arrange for follow-up testing. Nodules (shadows) on a CT scan can be different sizes and are calcified or non-calcified. Calcified nodules found on spiral CT are usually scars. They do not require further tests. Non-calcified nodules require follow-up CT scan or further tests (such as a biopsy). If a nodule(s) is(are) found on your CT scan, the size of the nodule(s) will determine when your next scan will be and if you need a biopsy or other test. We will be looking to see if the nodule changes size or shape to suggest it may be cancerous

How Long Will I be in this Research Study?

You will be in this study for 2 years. There are no follow-up tests planned after 2 years unless there is an abnormality in your CT scan or bronchoscopy that requires longer follow-up.

There is a table on the last page of this consent document that explains what will be done at each study visit and how long each visit will take.

The researcher may decide to take you out of this study due to lack of funding or if new information becomes available that may affect your decision to continue to participate in this study.

If any information becomes available during the study which may change your willingness to stay in the study, you will be informed of the information and asked if you want to continue participating. You may be asked to sign a new consent form indicating you want to continue in the study.

What Are the Risks of the Study?

Risk related to the lung cancer risk prediction tool:

On the average, a smoker with a similar smoking history as yours is at considerable increased lifetime risk of lung cancer. However, it is not yet known if our lung cancer prediction tool can pick out those with the highest risk. You could therefore be taking part in the screening studies (CT scan, bronchoscopy, spirometry blood test) while your lung cancer risk is not higher than the average current or former smoker. The risks of these screening tests are noted below.

Risks and side effects of blood draws and insertion of intravenous needle include:

Insertion of a needle into one of the veins in your arm to give the mild sedative and cough suppressant before your bronchoscopy and for the blood tests may cause pain, bruising or rarely, an infection of your skin. Rubbing alcohol used to clean your skin before taking the blood sample may cause redness of your skin.

Risk related to the Spiral CT scan:

The amount of radiation from a low dose CT scan is comparable to about 6 to 12 months of natural radiation exposure in the environment. If you have abnormality identified on your CT scan, you will have a follow-up low dose CT to rule out lung cancer. It is possible that you may have up to 4 low dose spiral CT scans in total over a 2 year period. No injury has been reported from the small amounts of radiation from a maximum of 4 CT scans related to this study. Finding a nodule on CT scan may lead to tests or surgery despite in the end being found not to have cancer. It may also cause some anxiety about a possible diagnosis of cancer.

Risks and side effects related to the bronchoscopies and biopsies:

Bronchoscopy is a standard clinical procedure and is considered to be of low risk. You may have a mild discomfort in your throat for a few hours to a couple of days afterward.

Local freezing (Lidocaine) has a bitter taste, and you will feel numb in your throat for about 1 to 2 hours after the bronchoscopy. Gagging or coughing may occur during the bronchoscopic examination despite the use of Lidocaine. Even if you are not known to be allergic to the medications you will receive, drug reactions may occur. Midazolam and Alfentanil may slow your breathing rate or drop your blood pressure. Because these drugs will be given in small doses as needed, and under close monitoring by a nurse throughout the procedure, the chance of this happening will be less than 1%.

Bronchial biopsy (taking a small sample of tissue during the bronchoscopy) may cause streaks of blood in your sputum (mucous that you might cough up) right after the bronchoscopy. Rarely (less than 1% chance), chills and a fever may occur a few hours after bronchoscopy. These conditions usually go away without treatment within 24 hours. However, if these symptoms are bothersome or continue for more than 24 hours, you should contact Dr. Lam or Dr. McWilliams immediately at (604) 675-8090 to rule out the rare chance of bronchitis or pneumonia.

Benefits

Studies are underway in the United States and Europe to find out if detecting (by screening individuals without symptoms hints of cancer) and treating lung cancer early in smokers will decrease the chance of dying from lung cancer. Until the results from these studies are available, it is not known if early detection (screening) would benefit you. However, your participation may benefit others in the future by helping us find out who is at greater risk of developing lung cancer and how best to screen for it.

Compensation

You will not be paid for participating in this study. The funding for this study is provided by the Terry Fox Research Institute. This organization is based on donated support and no funding has been provided to BCCA for reimbursement of extra costs such as parking. You will need to pay these extra costs yourself.

What Happens If I Am Injured Because I Took Part In This Study?

If you are injured as a consequence of participation in the study due to the study procedures, your medical condition will be evaluated. Medical care will be provided by one of the investigators or you will be referred for appropriate treatment. The costs of your medical treatment will be paid for by your provincial medical plan to the extent that such coverage is available.

No funds have been set aside to compensate you in the event of injury or illness related to study procedures.

You do not waive any of your legal rights for compensation by signing this form.

Remuneration

The Terry Fox Research Institute is the sponsor of this study. This institute reimburses the BC Cancer Agency for the costs of conducting this study. However, the investigators conducting this study will not receive any personal payments for conducting this study. In addition, neither the BC Cancer Agency nor any of the investigators or staff conducting this study will receive any direct financial benefit from conducting this study.

What Happens After The Study Is Finished?

You will not receive additional screening or follow-up tests after your participation in the study is completed unless there is any abnormality in your CT scan or bronchoscopy that requires medical follow up. Although you have completed the study, it is very important to find out if in future you develop lung cancer and what has happened after the cancer diagnosis. Even after your study participation is finished, we would still like to obtain information on your health to see how accurate the risk prediction tool was. We will continue to follow up on your health through the Provincial and National Cancer Registries, Vital Statistics and the provincial Medical Services Commission. A handout explaining the role of the Cancer

Registry will be given to you. There is an option at the end of this consent document for your permission to obtain these periodic updates.

If you develop lung cancer, the researchers of this study would like you to inform them, which you can do by contacting the study coordinator or study doctor.

Withdrawing From the Study

You can stop taking part in this study at any time. However, if you decide to stop taking part in the study, we encourage you to talk to the researcher and your regular doctor first. Your doctor may recommend follow up visits for abnormality on your CT scan or bronchoscopy.

If after signing this consent form, you decide to withdraw from the study or do not wish to participate in the periodic updates, you are asked to contact Dr. Lam or Dr. McWilliams at 604-675-8090 or 1-888-675-8001 local 8090 to inform them of your decision.

If you stop taking part in the study before completing all of the tests, any information or samples collected up to that point will still be used in analysis.

What Are My Rights as a Participant?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not affect the quality of your current or future medical care.

We will tell you about new information that may affect your health, welfare or willingness to stay in this study. You will also be advised of any new information that becomes available that may affect your willingness to remain in this study.

Who Do I Call if I Have Questions or Problems?

You are encouraged to ask any questions you may have about this study or about this information sheet. You will receive a copy of this information sheet for your records.

Dr. Stephen Lam or Dr. Annette McWilliams may be contacted at (604)675-8090 or toll-free at 1-888-675-8001 local 8090 at any time if you have questions regarding this study, if further information about the nature and conduct of this study is required, or if any problems result from your participating in this study.

If you have any concerns about your treatment or rights as a research participant you may contact the Research Subject Information Line at the UBC Office of Research Services at the University of British Columbia at (604)822-8598. On Vancouver Island, you may also contact Dr. Peter Kirk, Director of Research and Evaluation for the Vancouver Island Health Authority at (250)370-8261.

Confidentiality

Your confidentiality will be respected. No information that discloses your identity will be released or published without your specific consent. Your identity will not be used in any reports about the study. In records that leave this centre you will be identified by a study code only. Your birth date will also be provided if requested by the sponsor or responsible regulatory agency. All information associated with this study will be kept behind locked doors or in secure computer files.

Research records and medical records identifying you may be inspected in the presence of the Principal Investigator or his designate by representatives of the Terry Fox Research Institute, the UBC BCCA Research Ethics Board, the Vancouver Island Health Authority or Health Canada for the purpose of monitoring and checking the accuracy of the research. However, no records that identify you will be allowed to leave the centre. These organizations have policies of strict confidentiality and the individuals inspecting your records must sign a BC Cancer Agency confidentiality form. The confidentiality form is not applicable to Health Canada who has the legal right to inspect health records and are bound to confidentiality by specific laws.

Data from the questionnaires, CT scan, breathing test, blood test, bronchoscopy, reports concerning your progress and relevant portions of your study file, identified by a study code only, will be sent electronically to the central coordinating center of the study located at the BC Cancer Research Center. Information in these reports may include test results, reports of operations, x-rays, laboratory tests or imaging reports. The CT scan images, identified by a study code only will stored at the Radiology Department of the Vancouver General Hospital.

You will be identified by a study code only on any information created or collected in the course of your participation in this study. This is called anonymized information. All members of the Pan Canada Early Lung Cancer Study Group will collect anonymized information so that analysis of study data can take place. This collected anonymized information is entered onto an electronic database maintained by the central coordinating center at the BC Cancer Research Center. This anonymized information may be shared with other researchers in the Pan Canada Early Lung Cancer Study Group, sponsors of this trial, and/or the regulatory agencies that oversee such research. If some of the information is reported in published medical journals or scientific discussions, it will be done in a way that does not identify you.

Information that directly discloses your identity will remain only with the site Principal Investigator in Vancouver. Information that could be used to “link” your identity will not be released without your knowledge or consent unless required by law or regulation. You understand that by agreeing to participate in this study, anonymized information about you will be provided to the sponsor of this research study.

Your rights to privacy are legally protected and guaranteed by federal and provincial laws. These laws require safeguards to insure that your privacy is respected. You have the right of access to the information about you that has been provided to the sponsor and, if need be, an opportunity to correct any errors in this information. Further details about these laws are available on request to the investigator or the UBC BCCA Research Ethics Board.

Participant Consent

I understand that participation in this study is entirely voluntary. I may choose not to participate or I may withdraw from the study and/or the periodic updates at any time and I will continue to be offered the best available medical care. I understand that I may ask questions about this study in the future. I will receive a signed copy of this consent form including all attachments, for my own records. I understand that by agreeing to participate in this study, information about me, with my identifying information removed, will be provided to the sponsor of this research study.

a) I agree to participate in this study.

Yes _____ No _____ Initial _____

b) I agree to the periodic update of my health information using the Vital Statistics, Medical Services Commission and Cancer Registry databases as it relates to the research described in this document.

Yes _____ No _____ Initial _____

Participant's Signature Printed name Date

Witness' Signature Printed name Date

Signature of Person Obtaining Consent Printed name Date

Study Role

If this consent process has been done in a language other than that on this written form, with the assistance of a translator, indicate: Language: _____

Was the participant assisted during the consent process in one of ways listed below?

Yes No If yes, please check the relevant box and complete the signature space below:

The consent form was read to the participant, and the person signing below attests that the study was accurately explained to, and apparently understood by, the participant.

The person signing below acted as a translator for the participant, during the consent process.

Signature of Person Assisting in
the Consent Discussion

Printed Name

Date

The table below explains what will be done at each study visit:

This table does not describe additional tests that may be recommended and ordered if there is an abnormal finding on your CT scan or bronchoscopy.

| | |
|---|--|
| Prior to Registration | Informed Consent |
| Registration | <p>Questionnaires (Study Questionnaire, SF-12, EQ-5D and Anxiety Index) Body height and weight Breathing test (spirometry) Urine test (for former smokers only. To measure the amount of exposure to tobacco smoke) Spiral CT scan of the chest Autofluorescence bronchoscopy (first 1,250 participants only) Blood test (about 3 tablespoonfuls) Consent for optional storage of blood and tissues for future research</p> <p>The initial interview, breathing test and blood test will take about two hours. The CT scan will take about 15 minutes. The bronchoscopy will take about two and a half hours to three hours in total The CT scan and bronchoscopy will take place on separate days from the first appointment.</p> |
| Month 12 and 24 visit | <p>Blood test (about 2 tablespoonfuls) Breathing test (spirometry) Urine test (for former smokers only. To measure the amount of exposure to tobacco smoke) You will be asked if you have had other tests or treatment for lung cancer SF-12, EQ-5D and Anxiety Index Spiral CT scan of the chest (at the end of 12 months)</p> <p>The month 12 visit will take about one and a half hours. The month 24 visit will take about one hour. You will be asked to keep a written record of any tests or treatment for lung cancer.</p> |
| Month 6 and 18 telephone interview | <p>You will be asked if you have had other tests or treatment for lung cancer. You will be asked to keep a written record of any tests or treatment for lung cancer.</p> <p>The phone interview will take about 5 to 10 minutes each.</p> |
| Within 1 month after CT scan or bronchoscopy report | <p>Anxiety Index questionnaire.</p> <p>The questionnaire will take about 15 minutes. It will be completed over the phone after each CT scan or bronchoscopy report has been reviewed with you.</p> |

The total time needed (assuming you will also have a bronchoscopy) to participate in the study is estimated to be eight and a half hours over two years. This estimate does not include any extra tests/scans that may be required.