Letter of Information

Title: **XENON-129 MAGNETIC RESONANCE IMAGING OF HEALTHY SUBJECTS: HARDWARE AND SOFTWARE DEVELOPMENT AND REPRODUCIBILITY**

Sponsors: **Robarts Research Institute**

Protocol: **ROB0030**

Investigator: **Dr. Grace Parraga**

You are being invited to voluntarily take part in a research study. This letter of information has information to help you decide if you want to participate. Take your time, read this letter of information carefully, and ask the study investigator or staff any questions you may have. This study is being funded by CIHR (Canadian Institutes of Health Research). The study involves "Magnetic Resonance Imaging", or MRI, which is a non-invasive imaging technique that does not involve X-rays or ionizing radiation.

About This Study

The purpose of this study is to:

- Measure lung structure and function using a type of magnetic resonance imaging (MRI).
- Compare MRI of lungs with standard pulmonary function tests.

This type of MRI provides an opportunity to visualize, or "see" those areas of lung that are involved in ventilation and those that are not.

There may be reasons why you may not be eligible for the study. The study investigator or staff will discuss these with you.
This study is being conducted in one center, at the Clinical Imaging Research Laboratory, Robarts Research Institute. Approximately 100 people will be enrolled in the study over time. The study will end in 2031.

What will you be asked to do?

If you agree to participate in this study, you will be able to have up to 10 doses of ^{129}Xenon per year, and no more than 5 doses per visit at Robarts Research Institute, which is located next to University Hospital.

What will happen during the study visits?

When you come in for your study visits, the study investigator or staff may do the following:

Visit Information:

- Review your medical history and current medication(s).
- Take your vital signs (height, weight, blood pressure, heart rate, breathing rate and temperature).
- Perform lung function tests such as spirometry (test to measure how much air you can breathe in and out) as well as body plethysmography (a test which measures lung volumes) and diffusing capacity of the lung for carbon monoxide (DL_{CO}) (a test which measures lung function). For the body plethysmography test, you will sit in a closed Plexiglas chamber and breathe in and out into a mouthpiece.
- We will also measure lung clearance index and perform airway oscillometry, which gives us extra information about your lungs. Both of these tests involve breathing normally through a mouthpiece and take a few minutes to complete
- Perform a pulse oximetry test in which a clip is placed on your finger to measure the amount of oxygen in your blood.
- Assess your ability to hold your breath for 16 seconds.
- Perform an MRI using an inhaled gas (hyperpolarized xenon – ^{129}Xe). The MRI does not have radiation. One of three special coils will be placed around your torso and chest during the MRI. Either the CMRS Flexible Lung Coil, ^{129}Xe Lung Coil or ^{129}Xe Chest Coil will be used during the MRI. All of these coils are investigational devices that are not licensed in Canada but authorized for use in this study. These coils receive a signal from the magnet and helps to create the image. You will be asked to breathe in the gas from a special bag made for this procedure. You will be observed by a technologist during the entire procedure and may be spoken to through an intercom in the scanner.
- Perform a sputum induction procedure.
- Have a CT test (Computed Tomography) done at Robarts Research Institute. You will be accompanied by study staff to and from the imaging suite.
- These visits may take up to 2 ½ hours.
- You may be asked to wear a special nasal cannula during your scan that delivers oxygen.

What effects could the tests have on you?

You may feel discomfort during some of these tests and some may have risks, such as:

- Spirometry breathing tests may result in shortness of breath and light-headedness.
- Tests done in the body plethysmograph may cause claustrophobia, nausea, or vomiting.
- A sputum test measures eosinophils and neutrophils (a type of white blood cell) in your sputum. Eosinophils and neutrophils may be higher in the sputum of individuals with lung conditions.
  To obtain a sputum sample, you will inhale a salty mist that will help loosen secretions, or mucous from the chest so you can cough them up easily into a specimen container. You will inhale this mist for up to 7 minutes at a time for up to 3 times. You will be

asked to perform breathing tests during this process to make sure you may continue. You may stop at any time if you wish to.
Sputum samples will be analyzed by study staff at Robarts Research Institute. Please let study staff know if you would like to know the results of this test, or if you no longer want your samples to be used in this research.

- CT: You will receive a radiation dose in the CT scanner. The cancer risk related to this radiation dose is the same as the cancer risk related to smoking 23 cigarettes over your lifetime and the same as natural background radiation encountered over 2 months in London, Ontario.
- Part of your participation in this study will involve a research test with Magnetic Resonance Imaging (MRI) system, a common medical diagnostic tool that uses a strong magnetic field, a low frequency magnetic field, and a radio frequency field. No X-rays are used. As with any technology there is a risk of death or injury. For MRI the risk of death is less than 1 in 10 million and the risk of injury is less than 1 in 100,000. These risks do not arise from the MRI process itself, but from a failure to disclose or detect MRI incompatible objects in or around the body of the subject or the scanner room. It is therefore very important that you answer all the questions honestly and fully on the MRI screening questionnaire.

  Almost all the deaths and injuries related to MRI scans have occurred because the MRI operator did not know that surgically implanted metal hardware (such as a cardiac pacemaker) was present inside the subject during the MRI scan. Other remote risks involve temporary hearing loss from the loud noise inside the magnet. This can be avoided with ear headphone protection that also allows continuous communication between the subject and staff during the scan.

  For comparison, the risk of death in an MRI is similar to travelling 10 miles by car, while the risk of injury during an MRI is much less than the risks associated with normal daily activities for 1 hour.

  You may not be allowed to continue in this research study if you are unable to have a MRI scan because, for example, you have some MRI incompatible metal in your body, you may be pregnant or attempting to become pregnant, or you may have a drug patch on your skin that contains a metal foil. Should you require a medically necessary MRI scan in the future, the final decision as to whether you can be scanned will be made by a qualified physician considering all the risks and benefits.

MRI Exclusion Criteria

If you have any history of head or eye injury involving metal fragments, if you have some type of implanted electrical device (such as a cardiac pacemaker), if you have severe heart disease (including susceptibility to heart rhythm abnormalities), you should not have an MRI scan unless supervised by a physician. Additionally you should not have a MRI scan if you have conductive implants or devices such as skin patches, body piercing or tattoos containing metallic inks because there is a risk of heating or induction of electrical currents within the metal element causing burns to adjacent tissue.

About The Agent

Hyperpolarized xenon-129 (^{129}Xe) gas is an "investigational" agent that is used in MRI to better visualize (see) the lungs. "Investigational" means the study drug or study procedure has not yet been approved for clinical use by Health Canada. Health Canada has no objection to the use of Hyperpolarized xenon gas in this study. The agent has been approved by Health Canada for other procedures, and has been studied in over 2000 people worldwide, including about 150 participants in London Ontario.

What side effects can happen to you from inhaling hyperpolarized xenon gas?

Some adverse or bad side effects have been reported by people who have inhaled hyperpolarized ^{129}Xe gas for different procedures. The amount of gas inhaled by these people was approximately 70 times the amount you will be asked to inhale. The effects reported include respiratory depression (slow, shallow breathing) greater than 10 seconds (3.6%), seizures (0.2%), change in how you feel (0.1%), headache (0.4%), nausea and/or vomiting (0.2%) and change in sensorium (your senses may be affected) (0.1%). It should be noted that in the cases of seizure, 3 of the 4 patients who experienced seizures were being studied because they were having seizures, and the status of the 4th patient was unknown.

Each dose of ^{129}Xe is provided as a mixture by volume (35:65 or 50:50 depending on your lung size) mixed with medical Nitrogen in a 1 litre dose. This mixed gas dose is inhaled and mixed with the contents of your lungs and diluted 8 to 10-fold when inhaled. Therefore, each xenon dose is safe and can be repeated in a single visit. To ensure you do not become fatigued, we will limit gas inhalation to five doses per visit. While there is no yearly exposure safety limit we will limit the number of doses you might receive to 10/year so you are not fatigued by the process.

If you experience any side effects, please notify your study staff immediately.

It is not known what effects the MR scan or the xenon gas may have on an unborn baby. Therefore if you are a female of childbearing potential, you must be using an acceptable method of birth control in order to be enrolled in the study. The contrast gas has no effect on any future planned or unplanned unborn babies or on a partner of yours who may participate in the conception of a baby.

You will be told in a timely manner about significant new information that might affect your decision to stay in the study.

There may be other side effects or risks that are not known at this time.

If you are injured from the study procedure, who will pay the doctor and hospital bills?

If you are injured or become ill as a result of participating in this research study, the reasonable costs of medical treatment will be covered by the study's insurance policy, to the extent they are not covered by your medical or hospital insurance or governmental or other programs providing coverage. No other form of compensation is available.

You do not waive any legal rights by signing the consent form.

Voluntary Participation
Participation in this study is voluntary. You may refuse to participate, refuse to answer any questions or withdraw from the study at any time with no effect on your future care. You may be asked to leave the study without your consent if you need other treatment, have a study-related injury, or for any other reason.

What benefit could there be from taking part in the study?
Since this study does not provide treatment, there is no direct benefit to you. Information learned from the study may help other people with various types of lung disease in the future.

How will your privacy be protected?
By signing the Consent Form you agree that the study investigator and the regulatory agencies listed below may collect, use and disclose information about you. This may include your name, address, phone number, medical history and information from your study visits.

A file containing your information will be established by the principal investigator and maintained in connection with the study. Release of any information may include initials, date of birth, study number, and study visit dates.

Unless required by law, only the principal investigators and staff and inspectors from regulatory agencies including Health Canada will have direct access to your medical records to check the study information. Instead, it may include a study number and study visit dates. While we will do our best to protect your information there is no guarantee that we will be able to do so. The inclusion of your initials and date of birth may allow someone to link the data and identify you. If you think that you were harmed from being in the study, the research team may also share health data about you with the insurer to resolve your claim.
Your information will be kept strictly confidential as stated above. If the results of this study are published, no one will know you were a part of the study.

Representatives of The University of Western Ontario Health Sciences Research Ethics Board may require access to your study-related records or may follow up with you to monitor the conduct of the research.

Your study-related records will be kept for a period of 25 years as per Health Canada Regulations. You may take away your permission to use and share health data about you at any time by writing to the study investigator at the following address:

Dr. Grace Parraga
Robarts Research Institute
1151 Richmond Street North
London ON Canada N6A 5B7

You may also verbally withdraw your consent to participate in the study at any time. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after that date. However, health data about you that has already been gathered may still be used and given to others as described in this form.

When the study is over you may write to the study doctor to ask to see health data about you that was collected during the study.

If you decide not to sign the consent form, you will not be able to participate in the study.

Alternative to Study Participation
An alternative to the procedures described above is not to participate in the study and continue on just as you do now.

Will you be reimbursed?
You will receive $40.00 per study visit to reimburse you for travel and any other reasonable out of pocket expenses, which are directly related to your participation in the study. There will be no charge to you for any tests done as part of the study. If you are not able to complete all the visits in this trial you will be reimbursed for the visits you do complete.

Contacts

If you have any questions about your rights as a research participant or the conduct of this study, you may contact the Patient Experience Office at LHSC at (519) 685-8500 ext. 52036
If at any time you have any questions or need further information about this study, you may contact the study investigator, Dr. Grace Parraga at (519) 931-5265 or the study coordinator Angela Wilson at (519) 931-5777 Ext. 24197.

Consent Form

Title:	**Xenon-129 Magnetic Resonance Imaging of Healthy Subjects: Hardware and Software Development and Reproducibility**
Sponsors:	**Robarts Research Institute**
Protocol:	**ROB0030**
Investigator:	**Dr. G. Parraga**

I have read the Letter of Information, have had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction.

I will receive a signed and dated copy of the Letter of Information and Consent.

_____
Name of participant (please print)

_____
Signature of participant

_____
Date of signature

_____
Name of person obtaining informed consent

_____
Signature of person obtaining informed consent

_____
Date of signature