Letter of Information

Title: **Structure and Function MRI of Asthma**

Sponsors: **Robarts Research Institute**

Protocol: **ROB0037**

Investigator: **Dr. Grace Parraga**

You are being invited to voluntarily take part in a research study either because you have been diagnosed with Asthma" or you are a healthy volunteer. 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.

About This Study

The purpose of this study is to:

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

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 Robarts Research Institute. Approximately 120 asthmatics and 30 healthy volunteers will be in the study.

What will you be asked to do?

If you take part in this study, you will be asked to visit the clinic two times at Robarts Research Institute, which is located next to University Hospital. Each visit will take approximately 1 ½ to 2 hours. The second visit will take place 3 years after the initial visit. If you are one of the first 60 participants in the study, we will also ask you to visit the clinic after 2, 4 and 78 weeks. At these visits, we will ask you to do all the study procedures listed below.

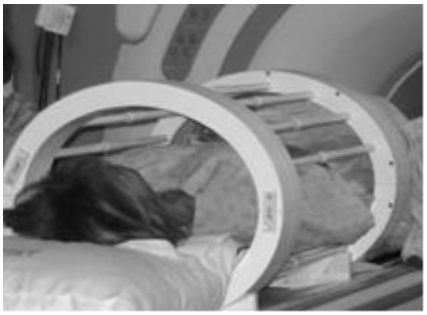
We will call you after 6 and 18 months to follow up and see how you are doing.

What will happen during the study visit?

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

- Take your vital signs (height, weight, blood pressure, heart rate, breathing rate and pulse oximetry test (a test in which a clip is placed on your finger to measure the amount of oxygen in your blood).
- You will be given 2-4 puffs of Salbutamol from an inhaler and an aerochamber. Salbutamol is a marketed bronchodilator which is used to open up the airways in patients with respiratory problems.
- Perform lung function tests such as spirometry (test to measure how much air you can breathe in and out) as well as body plethysmography and diffusing capacity of carbon monoxide (DL_{CO}) (tests of lung volumes and function). For the body plethysmography test, you will sit in a closed Plexiglas chamber and breathe in and out into a mouth-piece. This will take approximately 20 minutes. You will also perform Lung Clearance Index test during which you breathe normally into a mouthpiece for 3-5 minutes.
- Undergo a Methacholine challenge test:
    - The Methacholine test is performed by inhaling a medication (Methacholine) in increasing doses in an attempt to produce a change in your spirometry results. The test will continue until you reach at least a 20% drop in your FEV_1 (the amount of air you exhale in the first second) or you finish all the dosages of the medication.
    - After the testing is completed, you may be given Salbutamol ("Ventolin") that will reverse the action of the Methacholine, if it has caused your results to change.
    - After each dose and after the Salbutamol, you will be asked to perform several spirometry tests (a test that measures how much air you can breathe in and out)
- We will collect a small amount of sputum from you to measure inflammation in your airways. You will inhale a salty mist to try to loosen up some secretions from your chest so that you can cough them up into a specimen jar. This procedure takes approximately 30 minutes.

- Perform an MRI using an inhaled gas (hyperpolarized xenon – ^{129}Xe and/or helium-3 – ^{3}He). The MRI does not have radiation. A special coil will be placed around your torso and chest during the MRI. This coil receives a signal from the magnet and helps to create the image. You will be observed by a technologist during the entire procedure and may be spoken to through an intercom in the scanner.



MRI Coil

- Chest CT (Computed Tomography). This test will be done at University Hospital, located next door to Robarts Research Institute. You will be escorted to and from the radiology department by study staff.
- In between visits, we will ask you to complete some asthma questionnaires: one every week and another one every other week. We will ask you to upload these questionnaires monthly to our secure website using a confidential password. Instructions for these questionnaires will be given to you at your first visit by study staff.

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.
- The sputum induction process may cause gagging, coughing and a sore/burning throat, but these are usually not bothersome and they will not interfere with the test. Sometimes the procedure may cause you to hyperventilate and may cause some chest tightness and discomfort. You will do this test after you have inhaled salbutamol (Ventolin), which helps reduce the chance of chest discomfort.
- 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.

The MRI experiments carried out for this study are performed solely for scientific purposes The data which is collected is not optimized to make clinical diagnoses, and the research team involved in these experiments are not trained to make medical evaluations. By participating, you agree that the experimenters are not expected to arrive at a clinical interpretation of the data collected.

Nevertheless, there is a small possibility that a potential abnormality might be observed – otherwise known as an incidental finding. If this occurs you will be notified of the issue by the principal investigator of the study who will assist you with your options for following up. Investigators are not responsible for the outcome of medical follow-up or for any incurred costs during medical follow-up. By participating, you agree to the possibility of being informed about a potential incidental finding, according to the above-described procedure. If you do not agree to the potential risk of an incidental finding you should not participate in this study.

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.

- CT: The CT does deliver a radiation dose to your lungs which is similar to the dose for approximately 10 chest x-rays, or 10% of the same radiation dose you receive from the background radiation from the ground in London, Ontario over the course of a year.

About The Agents

^{3}He

Hyperpolarized Helium gas (^{3}He) is an “investigational” agent that is similar to the helium used in balloons, but 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 approved the use of Hyperpolarized Helium gas in this study. The agent has been studied in over 800 people worldwide.

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

Recent summaries of adverse or bad side effects have been reported by people who have inhaled hyperpolarized ^{3}He gas at a hospital research centre (University of Virginia in Charlotteville VA, USA); 10% had adverse side effects, all were mild and improved during the study without any treatment. Approximately 6% of people who have inhaled helium gas experienced side effects related to the dryness of

the gas and included: dry mouth or throat (3.5%), throat soreness (less than .005%), lung irritation (.005%), tickle in throat (less than .005%), chest tightness (.01%) and wheezing (less than .005%).

In similar studies sponsored by General Electric Health Care (the manufacturer of the ^{3}He hyperpolarized gas), 9% of all persons inhaling the gas had adverse side effects, all reported to be mild and improved during the study without any treatment. These side effects include breathlessness (4.5%), dry mouth (1.5%), throat pain (1.5%), throat irritation (0.75%), dizziness (0.75%), vague chest pain (0.75%) and bad taste in the mouth (0.75%).

^{129} Xe

Hyperpolarized Xenon gas (^{129}Xe) 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 approved 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 400 people worldwide.

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.

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

It is not known what effects the MR scan 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 does not interact with your body and therefore has no effect on an unborn baby, or 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 your provincial health care insurance. 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 asthma 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 study related information will be established by the principal investigator and maintained in connection with the study.

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.

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 Western University Health Sciences Research Ethics Board and Lawson Quality Assurance and Education Program 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 contacting the study investigator in person, by telephone or in writing at the following address:

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

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 letter.

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

Will you be compensated?

You will receive up to $50.00 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 clinic visits, or 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 or access the online form at: https://apps.lhsc.on.ca/?q=forms/patient-experience-contact-form.

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 & research nurse Danielle Knipping at (519) 931-5777 Ext. 24197.

Consent Form

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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