Protocol Title: Longitudinal MR Imaging of Pulmonary Function in Patients Receiving Thoracic Radiation Treatment

NCT02478255

Consent Reference Date: 26Apr2021

DUKE UNIVERSITY HEALTH SYSTEM

Consent to Participate in a Research Study
Longitudinal MR Imaging of Pulmonary Function in Patients

Longitudinal MR Imaging of Pulmonary Function in Patients Receiving Thoracic Radiation Treatment

You are being asked to take part in this research study because you are healthy and do not have lung disease, or you are scheduled to undergo Radiation Therapy (RT) for lung cancer, or other malignancies such as breast cancer or lymphoma that involve significant irradiation of the thoracic cavity. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As the study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate in this study, your doctors will be Drs. Joseph Mammarappallil, MD PhD and Christopher Kelsey, MD. They will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed. Please note that Dr. Driehuys, PhD is a meber of the study team and holds several patents related to the technology used in this study. These patents are licensed to Polarean, Inc for commercial development. While Polarean, Inc. is not sponsoring the present study, Dr. Driehuys does have an ownership stake in this company.

A grant from the National Institutes of Health (NIH) will sponsor this study. Portions of Drs. Mammarappallil's and Dr. Driehuys' salaries and their research team's salaries will be paid by this grant.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine whether magnetic resonance imaging (MRI) using inhaled hyperpolarized ^{129}Xe gas, and conventional contrast can help visualize impaired lung function and detect changes over time in patients receiving treatment as well as those who don't. ^{129}Xe is a special type of xenon gas and when inhaled during MRI may be able to show areas of abnormal thickening of parts of the lungs. These images combined with images taken with other special types of MRI such as ^{1}H MRI may provide a better way to look at lung structure and function. Our ultimate goal is to predict the degree of radiation-induced lung injury that will develop in a given patient for a given treatment plan. We anticipate that these images will provide more specific information about lung disease than standard lung function tests. The use of ^{129}Xe MRI is investigational. Investigational means that these tests have not yet been approved by the US Food and Drug Administration and are only available in research studies like this one.

Healthy volunteers are being asked to participate in this study because we need to develop a database of functional images that are representative of healthy lungs.

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HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
Approximately 35 participants consisting of 10 healthy volunteers and 25 patients scheduled to undergo thoracic radiation therapy will take part in this study at Duke University Medical Center.

WHAT IS INVOLVED IN THE STUDY?
If you agree to be in this study, you will be asked to sign and date this consent form. The study involves the following visits:

- Screening Visit – You will be asked to sign and date this consent form. At the screening visit, you will be asked for your medical history, record of medications, and your vital signs (including Hemoglobin (optional) Finger sensor machine) will be measured . You will be asked to fill out a questionnaire to ensure that you are eligible to undergo an MRI scan. If you are female of child-bearing potential, you will be required to undergo a serum pregnancy test and it must be negative before you can continue to participate in this study.

- Visit 1 - Baseline imaging study. If you are a healthy volunteer, this visit will take place at the same time as the screening visit or shortly after and will be your only study visit. If you are a subject that is about to begin thoracic radiation therapy, this visit may also occur at the same time as the screening visit or shortly after, but must be done before you begin radiation therapy.

- Visit 2- Ten to fourteen weeks after Radiation Therapy is completed.

- Optional Visit 3 Thirty-two to forty weeks after Radiation Therapy is completed.

- Please initial one of the options below to indicate you are willing to be contacted for visit 3

- ____ Yes, I agree to be contacted for the optional visit 3, thirty-two to forty weeks after Radiation Therapy is completed.

- ____ No, I do not agree to be contacted for the optional visit 3, thirty-two to forty weeks after Radiation Therapy is completed.

Each of these visits will take about 4 hours. Each visit will begin with a review of your relevant history, symptoms, medications and rescreening for eligibility to participate, including a serum sample for pregnancy testing for women of child-bearing potential and your vital signs (including optional hemoglobin by finger sensor) will be measured. Either after screening or on a separate day you will undergo pulmonary function testing to assess your global lung function using standard clinical tests. However, if pulmonary function test results are already available from your medical record, the pulmonary function tests will not be done.

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After pulmonary function testing you will participate in the MRI portion of the study. For the MRI examination, you will lie on your back on a table, wearing a vest that transmits and receives signals for the MRI and a small sensor will be applied to your finger to monitor your pulse rate and blood oxygen levels. The table will be slid into the bore of the MRI scanner (a tunnel about 6 feet long and 25 inches in diameter) and we will obtain one or more MRI scans of your lungs. After this, you will be instructed to inhale a small calibration dose of hyperpolarized ^{129}Xe from a plastic bag through a mouthpiece. Following this, you will be asked to inhale additional doses of hyperpolarized ^{129}Xe to acquire different kinds of lung scans. For each ^{129}Xe dose you will be asked to hold your breath for approximately 15 seconds while the scan is obtained. During each scan, your heart rate and your oxygen saturation will be monitored. After each ^{129}Xe dose, the table will slide out of the MRI bore so that you can communicate with study personnel. When you are ready, the next xenon dose will be administered. Following ^{129}Xe MRI, you will be fitted with a different MRI coil vest for high-resolution imaging of your anatomy.

After the MRI examination, you will remain with study personnel until you feel recovered from any study effects and your heart rate and oxygen saturation are within an acceptable range. You will then be free to go home. The study coordinator will give you her contact information at the time of your initial visit. If you feel that you are having any symptoms or effects related to your participation in the study, please contact the study coordinator or the physicians listed in this consent.

In addition, the team may obtain information from your DUHS medical record and use this data to analyze the MRI scans obtained as part of this study. The study doctor may stop your participation in this study at any time without your consent. Potential reasons for ending your participation may include safety concerns or general reasons related to the conduct of the research study itself.

HOW LONG WILL I BE IN THIS STUDY?

Your participation in the study will require about 4 hours for each visit depending upon whether or not your screening, pulmonary function testing, and imaging sessions are performed on the same day. If you are a healthy volunteer it may require only a screening visit and an MRI study visit. That decision will be made by you and the study personnel based upon your availability and that of the MRI scanner. Subjects who are undergoing thoracic radiation therapy will be in the study from the time this consent form is signed until the completion of the study visit 2; they will be given the option to participate in visit 3. For patients who participate in 2 visits, their participation will last until approximately 4 months after RT is completed, while patients completing the optional 3rd visit will participate until 12 months after RT.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. If you decide to stop participating please notify the study team by *Joseph Mammarappallil,*

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MD PhD at (919) 684-2051 during regular business hours or *at (270) 232-6617) after hours or on weekends*.

Note: in the event of scan cancellation for any reason or inadequate image quality, you may be asked to return for a single repeat scan (and additiona reimbursement). We anticipate this will happen in less than 5% of the cases.

WHAT ARE THE RISKS OF THE STUDY?
There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential information but this cannot be guaranteed.

Venipuncture – Taking blood from a vein in your arm by needle stick
Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely.

MRI Risks:
Magnetic resonance imaging (MRI) uses a magnet and radio waves to make diagnostic medical images of the body. There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. However, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will be excluded from participation in this research study.

The study involves entering a large room in which a magnet is present. You will be placed on a narrow bed and then slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will be asked to lie still for about one hour on this bed. During MRI scanning you will hear a loud machine-like noises. You may be asked to have a harmless monitoring device applied during the study. During the study, you can have voice contact and physical contact with someone in attendance if you desire. The MRI scan can be stopped at any time if you request it.

Risks of Xenon Gas:
Inhalation of xenon gas may cause you to feel the following effects:

- Slight numbness in the legs
- Nausea
- A sensation similar to smelling flowers
- A feeling of well-being or elation
- Mild tingling in the fingertips

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Female
Being a part of this study (MRI) while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman of childbearing potential, you will be required to undergo a serum pregnancy test and it mus be negative before you can continue to participate in the study. A urine pregnancy test will also be completed on the day of your MRI if done on a different day from screening and/or other study visits. For the duration of the study you agree to use an approved method of birth control. Medically acceptable contraceptives include: (1) surgical sterilization (such as a tubal ligation or hysterectomy), (2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) an intrauterine device (IUD). Contraceptive measures such as Plan B (TM), sold for emergency use after unprotected sex, are not acceptable methods for routine use. If you do become pregnant during this study or if you have unprotected sex, you must inform your study physician immediately.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
This research study is not an established diagnostic medical test and will be of no direct benefit to you. We hope that in the future the information learned from this study will benefit other people with lung disease. The pictures obtained during this study are for research purposes and are not designed to search for any existing lung, heart, abdominal, or other abnormalities. In the unlikely event that the technologist or investigator evaluating your scans notices something that appears abnormal, these scans will be reviewed by a radiologist, and the results of his/her evaluation will be provided to you and/or your primary care physician. The decision to proceed with any further evaluation or treatment based upon this information lies with you and your physician. If you choose to pursue further evaluation or treatment, you will be responsible for any additional costs incurred.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests, x-rays, and procedures may be reported to National Institutes of Health (NIH) and its affiliates. These could include pulmonary function tests and MRI scans of the lungs. In addition, the team may obtain information from your DUHS medical record and use this to analyze the MRI scans obtained. The date and time included in

your MRI will be stored on the images indefinitely. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Food and Drug Administration], representatives and affiliates of NIH, the Duke University Health System Institutional Review Board, [the Duke Cancer Institute, Duke Ethics and Compliance Office and other authorized organizations], and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record.
The study results will be retained in your research record forever. Any research information in your medical record will also be kept indefinitely.

This information may be further disclosed by the sponsor of this study. If disclosed by the sponsor, the information is no longer covered by federal privacy regulations.
If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

The Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);
2) you have consented to the disclosure, including for your medical treatment; or
3) the research information is used for other scientific research, as allowed by federal regulations protecting research subjects.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the Food and Drug Administration (FDA).

You should understand that a Confidentiality Certificate does not prevent you or a member of your

family from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

WHAT ARE THE COSTS?
There will be no additional costs to you as a result of being in this study and there is no charge for the MRI scan. However, routine medical care for your condition (care you would have received whether or not you were in this study) will be charged to you or your insurance company. You may wish to contact your insurance company to discuss this further. In order to make sure that tests and studies done solely for research purposes are charged correctly, we will carefully monitor your Duke Hospital and Clinic charges as long as you are participating in this study. These tests and studies are not a part of routine care, and people who are not part of the study do not usually have them performed. Please ask your study personnel if you would like to know more about which tests and studies are being done solely for research purposes.

WHAT ABOUT COMPENSATION?
You will be reimbursed for your time and expenses related to your participation as follows:
Screening V1 $50
Imaging V1 $50
V2 $100
V3 $100

Please note that payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual exceeds $600 in any one calendar year, Duke University is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of Duke University exceeding $600 during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the IRS.

WHAT ABOUT RESEARCH RELATED INJURIES?
Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury.

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For questions about the study or research-related injury, contact *Joseph Mammarappallil, MD PhD at (919) 684-2051 or Bastiaan Driehuys, PhD at (919) 684-7786* during regular business hours. After hours and on weekends and holidays, contact *Dr Joseph Mammarappallil, MD PhD at (270) 232-6617 or Bastiaan Driehuys, PhD at (919) 923-1981*.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?
You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. Nonparticipation or withdrawal from this study will not affect your job status if you are a Duke employee and will not affect your grades if you are a Duke student. If you do decide to withdraw, we ask that you contact Dr. Driehuys in writing and let him know that you are withdrawing from the study. His mailing address is DUMC Box 3302, Durham, NC 27710.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or research-related injury, contact *Dr Joseph Mammarappallil, MD PhD at (919) 684-2051 or Bastiaan Driehuys PhD at (919) 684-7786* during regular business hours. After hours and on weekends and holidays, contact *Dr. Joseph Mammarappallil, MD PhD at (270) 232-6617 or Bastiaan Driehuys, PhD at (919) 923-1981*.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the Duke University Health System Institutional Review Board (IRB) Office at (919) 668-5111.

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

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S.Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

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STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time.
I have been told that I will be given a signed and dated copy of this consent form."

_____ _____/_____
Signature of Subject Date Time

_____ _____/_____
Signature of Person Obtaining Consent Date Time