Informed Consent Form

RAD4267-17: A Pilot Study of FDG-PET Variability to Establish Biology-Guided Treatment Planning Feasibility for Stereotactic Body Radiation Therapy (RefleXion)

NCT Number: NCT03493789

Document IRB Approval Date: 11/5/2018

You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

A Pilot Study of 18F-FDG PET Variability for Use in Emission-Guided Stereotactic Body Radiation Therapy Planning

Principal Investigator: Kristin Higgins, MD

Sponsor: RefleXion Medical

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision with your friends and family. You can discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation. You are being asked to take part in this study because you are being considered for a specific type of radiation treatment called stereotactic body radiation therapy as part of your cancer treatment.

Introduction

This consent form is part of an informed consent process for a research study and it will provide information that will help you to decide whether you wish to volunteer for this research study. It will help you to understand what the study is about and what will happen in the course of the study.

If you have questions at any time during the research study, you should feel free to ask them and should expect to be given answers that you completely understand.

After all of your questions have been answered, if you still wish to take part in the study, you will be asked to sign this informed consent form.

The study doctor or another member of the study team will also be asked to sign this informed consent. You will be given a copy of the signed consent form to keep.

You are not giving up any of your legal rights by volunteering for this research study or by signing this consent form.

Why is this study being done?

This study is being done to better understand how we can treat cancer with radiation therapy. In this study we are gathering more information about your tumor to determine whether there are better ways of giving radiation therapy. This is done by obtaining imaging tests known as PET scans, which is a test that you may already had done before. We will use the information from your PET scans together with the details from your radiation treatment, such as how much dose is being given to the tumor, to figure out whether a new way of giving radiation is possible. This new method of radiation therapy would potentially use PET activity to guide

radiation delivery, which is the reason several PET scans are part of this study. Your radiation treatment would not change in any way by participating in this study.

How many people will take part in the study?

About 20 patients will participate in this study. They will all be receiving the same type of radiation therapy as you. They may have different types of cancers. This has been designed so that we can gather enough information from patients with different types of cancers.

How long will I be in the study?

We estimate that you will be part of this study for no more than 6 weeks. This includes your first visit with your radiation oncologist, enrolling on the study, to the end of your radiation therapy course. During this period, as part of the study, you will participate in getting up to 3 additional PET scans, which are spread out over several visits, and will take place before and during your radiation course.

Can I stop being in the study?

Your participation in your clinical trial is completely voluntary. You can stop participating at any time. If you decide not to participate it will not affect your medical care at Winship Cancer Institute. If you join this study you may withdraw from it at any time. However, if you decide to withdraw from the study, we encourage you to talk to your research doctor first. A reason to tell your doctor that you are thinking about stopping is to discuss what follow up care and testing could be most helpful for you.

Why have I been asked to take part in this study?

You have been asked to participate in this study because you have been recommended by your radiation oncologist to receive a type of radiation known to stereotactic body radiation therapy (SBRT) to lung or other types of tumors. This is a type of treatment that used very focused radiation that is given over five treatments. You have been asked to participate on this study because we are interested in studying ways to improve this type of radiation therapy, and based on other factors of your cancer that make you eligible.

What will happen if I take part in this study?

Patients are candidates for this study if they have been recommended by their radiation oncologist to receive a type of radiation called to SBRT to lung tumors or other tumors. Patients should receive this treatment as outlined by their doctor.

As part of this study, you will be asked to participate in up to 3 additional PET scans. These PET scans will be taken in the Department of Nuclear Medicine at Emory University Hospital. The first PET/CT scan should be taken before you start radiation treatment; and we would like this study to be done within 2 weeks of enrolling on the study, or within 4 weeks of actual radiation therapy. You may have had this type of study already done in preparation for radiation therapy. If this study has been done within the time frame, and meets certain technical requirements, you will not have to get an additional PET scan before start radiation. The next PET scan will be taken after your first radiation treatment, and before the second treatment. The

final PET scan will be taken before the final radiation treatment. These tests can take place either on the same day as your radiation therapy immediately prior to your treatment, or on the day before. If you are recommended to have other types of treatment, such as chemotherapy, immunotherapy, hormonal therapy, or surgery, they are allowed as part of this study, as long as it does not interfere with your recommended radiation therapy or ability to get the PET scans.

What are the risks of the study?

You may have side effects while on this study. Most of the side effects are listed here. But there may be other side effects that we cannot predict. Side effects can be different from person to person. Everyone who is taking part in the study will be carefully watched for any side effects. Side effects can be mild, or in rare cases, serious. Your health care team may give you medications to help reduce some of the side effects. Most side effects will be temporary, and will go away soon after the treatment is over. Generally, side effects associated with PET scans is minimal and the risk of a serious side effect is very rare.

You should talk to your study doctor about any side effects that you may have while taking part in the study.

For your PET scan, a small amount of radioactive material will be injected by either a hand-held needle or a machine. Such injections are generally quite safe, but any injection involves some risks. The injection could harm a nerve, artery or vein, or cause infection. The radioactive material could also leak from your veins a little, causing swelling and discomfort. After injection and a waiting period for the drug to circulate within your body, you will be asked to lie very still for several minutes while the scan takes place.

If you are a woman and have undergone less than radical surgery (i.e. uterus/ovaries still intact): to protect against possible side effects of the radiation therapy, women who are pregnant or nursing a child may not take part in this study. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

Radiation-related risks

In addition to radiation therapy you may receive additional radiation from diagnostic procedures to evaluate your condition. The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. However, the additional risk of radiation-induced cancer from these diagnostic procedures is low compared to the risks from the radiation therapy.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Are there benefits to taking part in the study?

Taking part in this study will not impact your cancer treatment. You will receive the treatment that has been recommended by your radiation oncologist. If you decide to participate in this study, there will not be a direct medical benefit to you. However, we will have additional information about your tumor from PET scans, and

the information that we gain from this study could help patients with cancer undergoing a similar treatment in the future.

Who owns my study information?
If you join this study, you will be donating your study information. You will not receive any compensation if your information is used to make a new product. If you withdraw from the study, data that was already collected may be still be used for this study.

Will I be compensated for my time and effort?
You will not be offered compensation for being in this study.

What other choices do I have if I do not take part in this study?
You may choose to not participate in this study. Other treatments that you may consider for your cancer include the following:

- Getting treatment or care for your cancer without participating in a study
- Taking part in another study for your cancer
- Getting no treatment other than close observation and follow-up, treatment that only improves your symptoms

Talk to your doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?
By participating in this study, you should understand that we would be collecting personal health information. All efforts will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. The study data will be collected, and maintained electronically. The information collected during study visits, including PET scan data and radiation treatment details will be entered into a study database, which can only be accessed by certain members of the study team. Your personal identity, meaning your name, address, and any information that can identify who you are, will remain confidential. This is done by using a study number instead of your actual name. Only the study doctor, certain members of the study team, and study monitors will be able to link the study number to your name. Your data will also be forwarded to the study sponsor, RefleXion Medical. They will analyze the information from your PET scans and radiation plan for research. If the findings from the study are published, you will not be identified by name.

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information
De-identified data from this study may be shared with the research community at large to advance science and health. Data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or

code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory Healthcare medical record you have now or any time during the study.

Emory Healthcare may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory Healthcare medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include: None.

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory will help you get medical treatment. Emory and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Kristin Higgins at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

What are the costs of taking part in this study?

This study will not affect your cancer treatment with radiation therapy; it is not designed to change how you will receive your cancer care. You and/or your health insurance company will need to pay for the cost of treating your cancer with radiation therapy in this study. Some health insurance plans may not pay for these costs for members taking part in studies. Please check with you insurance company to find out what they will pay for. Taking part in this study may cost your insurance company more or less than the costs of getting

cancer treatment. Please ask your insurance company about the expected costs. The additional PET scans that are part of this study will be covered by the study sponsor, Reflexion Medical. You will not be paid for participating in this study.

The study sponsor will pay for certain items and services that you may receive if you take part in this study.

You will have to pay for the items or services for which the study sponsor does not pay. The sponsor will not pay for your regular medical care. If you have insurance, Emory will submit claims to your insurance for items and services that the sponsor does not cover. Emory will send in only those claims for items and services that it reasonably believes your insurance will pay and that the sponsor has not paid.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and the sponsor will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's website at http://cancer.gov/clinicaltrials/learningabout/payingfor.
You can print a copy of the "Clinical Trials and Insurance Coverage" information from this website. Or you call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a copy.

What will happen if you do not wish to take part in the study or if you later decide not to stay in the study?

Participation in this study is voluntary. You may choose not to participate or you may change your mind at any time.

No matter what decision you make, there will be no penalty to you and you will not lose any of the benefits you are otherwise entitled to. Leaving the study will not affect your medical care. You can still get your medical care from our institution, your relationship with the study staff will not change.

The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for study.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. **Use and Disclosure of Your Information That is Required by Law**:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study or receive research-related treatment. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study and give you study related treatment.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- RefleXion Medical is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.

- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Food and Drug Administration
    - Public health agencies
    - Research monitors and reviewer
    - Accreditation agencies
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Kristin A. Higgins, MD
Department of Radiation Oncology
Winship Cancer Institute of Emory University
1365 Clifton Road NE
Atlanta, GA 30322
(404) 778-3473

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. The Sponsor, and people and companies working with the Sponsor on this study are not covered by the Privacy Rules. They will only use and disclose your information as described in this Consent and Authorization.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Where can I get more information? Who can answer my questions about the study?
You may call the NCI's Cancer Information Service at
1 800 4 CANCER (1 800 422 6237)

Visit the NCI's Web site at http://cancer.gov/
For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

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. You will get a copy of this form. You may also request a copy of the protocol (full study plan).

Contact Information
Contact Kristin A. Higgins, MD at [redacted]:

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at [redacted]:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent and Authorization

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the study.

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____ ____:____ am / pm
Signature of Subject (18 or older and able to consent) Date Time (please circle)

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____ ____:____ am / pm
Signature of Person Conducting Informed Consent Discussion Date Time (please circle)