Study Title: Non-invasive, MRI-based assessment of tumor hypoxia to guide hypoxia-driven adaptive radiation therapy.
Version Date: 02/10/2024
PI: Jill B. De Vis, MD PhD NCT05996432

Name of participant:_____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:
You are asked to participate in this study because you were recently diagnosed with cancer of the head and neck region, or cancer that has spread to the brain. The goal of the study that you are asked to participate in, is to develop a magnetic resonance imaging (MRI) sequence that can evaluate the amount of oxygen that goes towards cancer cells. We believe that the development of such an imaging tool is of importance as the amount of oxygen that goes towards cancer cells may predict their response to treatment.

As a Participant in this study, you will get two research magnetic resonance imaging (MRI) scans and two research positron emission tomography (PET) scans. Participants diagnosed with head and neck cancer will get one MRI and one PET scan before the start of their radiation treatments, and one MRI and one PET scan at approximately one to two weeks into radiation treatments. Participants with brain metastases will get one MRI and one PET scan before their radiation treatments, and one MRI and one PET scan at approximately 3 months after their radiation treatments.
This MRI scan will take about an hour, and we will not give you any contrast agent for this MRI scan. The PET scans will take about 3 hours.

You, as a participant in this study, will not benefit from this study, but the data obtained in this study may help us optimize radiation treatments of future patients.

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Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you were diagnosed with cancer of the head and neck region or cancer that has spread to the brain. The latter is also known as brain metastases. Both head and neck cancer and brain metastases can be treated with radiation. Previous research studies have shown that the amount of oxygen that goes towards cancer cells prior to their radiation treatments, predicts how the cancer cells will respond to radiation treatment. Unfortunately, there is no established, non-invasive technique available that measures the amount of oxygen that goes towards the cancer cells. Only highly specialized PET scans that use 18F-fluoromisonidazole (18F-FMISO) as a radiotracer, which is a radiotracer that is not available in most hospitals, can measure this. However, in the last few years, researchers at Vanderbilt University Medical Center have worked on the development of non-invasive MRI techniques that can either measure the amount of oxygen in tissue, or MRI techniques that measure parameters related to the amount of oxygen that goes towards the brain. These techniques can also be used to derive the amount of oxygen that goes towards the cancer cells, but it has not yet been determined which one of these techniques is most sensitive to predict the response of cancer cells to radiation treatments. The goal of this study is to evaluate just that, by comparing the MRI results to the results of the specialized PET scan.
In this study, the MRI and PET scans are for research only. But, if we see something that is not normal, you will be told and asked to consult your doctor.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:
There are no known major risks with an MRI scan. But it is possible that harmful effects could be found out in the future. Even though the tunnel is open, it may bother you to be placed in a tight space (claustrophobia), and to hear the noise made by the magnet during the scan. You will be given earplugs to reduce the noise. You may also feel the table vibrate and/or move slightly during the scan. It may be

hard to lie on the table during the scan. If you have any metal pieces in your body, they could move during the scan and damage nearby tissues or organs.

If you use a transdermal patch (medicated patches applied to the skin), you may need to take it off during the MRI scan. Transdermal patches slowly deliver medicines through the skin. Some patches have metal in the layer of the patch that is not in contact with the skin (the backing). You may not be able to see the metal in the backing of these patches. Patches that contain metal can overheat during an MRI scan and cause skin burns in the immediate area of the patch. Tell the study doctor that you are using a patch and why you are using it (such as, for pain, smoking cessation, hormones). Ask your doctor for guidance about removing and disposing of the patch before having an MRI scan and replacing it after the procedure. Tell the MRI facility that you are using a patch. You should do this when making your appointment and during the health history questions you are asked when you arrive for your appointment.

There are no known risks of having MRI scans without contrast while pregnant. However, there may be risks that are unknown. For that reason, we will not allow participants who are pregnant or who think that they may be pregnant into this study.

You are agreeing to participate in a research project that involves the use of imaging procedures that expose you to radiation. This section will discuss the risks associated with the imaging procedures that are for research only. Your doctors may order additional imaging procedures as part of your normal patient care that also expose you to radiation. Those normal imaging procedures are not included in the risk discussion below. Please discuss those procedures and radiation risks with your doctors. As part of this research study, you may be asked to have additional imaging procedures that involve the use of ionizing radiation in the form of x-rays (for computed tomorgraphy or CT) and as an injection of a radioactive substance into your body (for PET or positron emission tomography). The amount of radiation that you could receive, should you have all of the imaging procedures is approximately 50% (or about ½) of the amount allowed annually for persons exposed to radiation as part of their work. Additionally, to protect your bladder from the effects of the injected radioactive substance, you should drink plenty of fluids and empty your bladder every two hours for at least the first six hours after you have the PET/CT scan.

All efforts, within reason, will be made to keep your personal information in your re-search record confidential, but there is always a potential risk of a breach of confidentiality that you should be aware off.

The following potential adverse effects are considered extremely rare:
-Risks related to allergic reaction that may be life threatening

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-Injection related risks that may include infection, or extravasation of the dose that may lead to discomfort, localized pain, temporary loss of local function, and self-limited tissue damage.

Risks that are not known:
There may be risks that we do not know about at this time, if we see something that is not normal, you will be told and asked to consult your doctor.

Regarding pregnancy, there have been no appropriate studies that either rule out or demonstrate negative effects of MRI on fetuses and therefore if you are pregnant, you will not be eligible for this study.

Good effects that might result from this study:
While you will not benefit directly from this study, the benefits to science and humankind that might result are identifying the MRI sequence that most accurately predict response of cancer cells to radiation treatments. In the future, this information may be used to personalize radiation treatments and increase their efficacy.

Procedures to be followed:
For this study you will undergo one MRI scan in the days prior to your radiation treatment(s). The MRI scan that you will be getting as part of this study will take about 60 minutes, and you will not get any contrast agent during this MRI scan. An MRI scan is taken in a large machine that is shaped like a tunnel. This scan does not use x-rays. Instead, they use a strong magnet and radio waves, like those used in an AM/FM radio to make pictures of your body.

You may not be able to have this scan if you have a device in your body such as aneurysm clips in the brain, heart pacemakers or defibrillators, and cochlear implants. Also, you may not be able to have this scan if you have an iron-based tattoos, pieces of metal (bullet, BB, shrapnel) close to or in an important organ (such as the eye). Prior to the MRI scan, you will be asked to fill out a metal screening form to ensure that you are eligible for an MRI.

Certain metal objects like watches, credit cards, hairpins, writing pens, etc. may be damaged by the machine or may be pulled away from the body when you are getting the scan. Also, metal can sometimes cause poor pictures if it is close to the part of the body being scanned. For these reasons, you will be asked to remove these objects before going into the room for the scan.

You will hear "hammering", clicking, or squealing noises during the scan. You will be given earplugs to reduce the noise. You will also be told how to alert the staff if you need them.

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During the scan, the MRI staff is able to hear and talk to you. You will also be able to hear the staff. They will be talking to you during your scan and may ask you to hold your breath, not move, or other simple tasks. You may be asked to lie very still throughout the scan. During the scan, the MRI staff will also be collecting your arterial oxygen saturation by applying an oxygen monitor around one of your fingers.

You will be getting two PET scans as part of this research study. These PET scans will take about 3 hours and will take pictures of your body after a radioactive metabolic tracer has been given. The tracer is injected into a vein within your hand or arm. The tracer will then collect in areas of your body that have low levels of oxygenation. The PET images will be combined with a computed tomography (CT) scan.

As part of this study, study personnel will review your medical chart up to 3 times; once at study enrollment and a second and third time one and two years following your MRI scan. During this chart review, we will retrieve your demographic information, your past medical and family history, as well as review the reports of your clinically indicated imaging scans.

Costs to you if you take part in this study:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payments for your time spent taking part in this study or expenses:
For each study visit that is not on the same day as one of your clinic visits, you will be reimbursed for mileage from your home to the hospital, at the federal mileage reimbursement rate.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

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There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Dr. Jill B. De Vis [redacted]

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
If you are unable to complete the MRI, you will be excluded from this study. This will not affect any other healthcare you might receive.

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Confidentiality:
All efforts, within reason, will be made to keep your personal information in your research record confidential but total confidentiality cannot be guaranteed. Your data will be stored both on digital media (which will not leave the secured scanner area) and on the Institute of Imaging Science server, which is protect by institutional firewalls and is password protected. Investigators may archive these data for their own use, in which case they will be kept in the relevant investigator's locked office.

In compliance with National Institutes of Health (NIH) data sharing initiative, imaging data without any personal information attached may be shared with other investigators or public data repositories, which provides the research community with open access to data sets contributed by labs around the world. Information will be completely anonymized with demographics limited to age (accurate to the year up to 90 years old, "90+" for older individuals, gender (male, female), and group membership (e.g., disease/treatment state). Data will be transferred using secure file transfer protocols. Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. De Vis and other researchers involved in this study will comply with any and all laws

regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information. This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means. It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help. Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:
Any information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your data. These tests may help us, or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:
There are no plans of sharing study results directly with you at this time, but you may reach out to the study personnel once study is published and be directed to any publications resulting from this data.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use, or share the information?
The people who may request, receive, or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors,

government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you canceled your authorization.

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds this data. To ensure the scientific quality of the research study, you will not be able to review some of your research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

Participation in future research studies.
As a result of the facts we get from this study, you may be asked to be in future studies. Please read the choices below and mark the one that is best for you.

I would like to be contacted regarding future research at Vanderbilt University which the investigators find me eligible. I understand that I am in no way obligated to participate, but I would like to give Dr. Jill De Vis and other research personnel involved in this study the permission to contact me about future studies.

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□ Yes □ No

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STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date _____ Signature of patient/volunteer _____

Consent obtained by:

Date _____ Signature _____

Printed Name and Title _____

Time: _____