TITLE OF RESEARCH STUDY:

Title: In vivo molecular imaging (MRI) of atherothrombotic lesions

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

Name: Dr. Zahi Fayad

Physical Address: Translational and Molecular Imaging Institute, Icahn School of Medicine at Mount Sinai, Hess Center for Science and Medicine, New York, NY 10029

Mailing Address: One Gustave Levy Place, Box 1234, New York, NY 10029

Phone: (212) 854-8452

WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don't know enough about. Participating may not help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care within the Mount Sinai Health System.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

Basic information about this study will appear on the website http://www.ClinicalTrials.gov. There are a few reasons for this: the National Institutes of Health (NIH) encourages all researchers to post their research; some medical journals only accept articles if the research was posted on the website; and, for research studies the U.S. Food and Drug Administration (FDA) calls "applicable clinical trials" 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.

PURPOSE OF THIS RESEARCH STUDY:

The purpose of this study is to test an investigational method of imaging (taking pictures) of atherosclerosis in your arteries. Atherosclerosis is a disease that builds fat deposits inside your arteries. We are investigating whether MRI and PET imaging can be used for imaging this disease in your blood vessels and cardiovascular system (heart and blood vessels). Both MRI and PET imaging are FDA approved tools for imaging the body however they are not currently routinely used for imaging atherosclerosis.

You may qualify to take part in this research study because you have some degree of atherosclerosis or if you or any of your family members have risk factors for atherosclerosis. Alternatively, you may have one or more newly emerging risk factors for cardiovascular disease such as acute or chronic inflammatory disease (e.g. an inflammatory skin condition such as dermatitis), or the use of e-cigarettes, that are thought to be related to risk of atherosclerosis. You may also qualify as a normal control subject who does not have atherosclerosis or risk factors, but is otherwise comparable to someone else in the study who does have atherosclerosis with whom we can compare the results of the imaging tests to determine how well the tests work. You may have been asked to participate before and after a surgical or other procedure. If this is the case, the timing of the scans in relation to the procedure will be explained by a member of the research team. This will also be explained in writing in an additional patient information leaflet. The imaging performed will only be done for the purpose of this research study.

Funds for conducting this research are provided by the National Institute of Health (NIH).

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Your participation in this research study is expected to last from 1 day to 5 years depending on which parts of the study you participate in. Each scan you participate in will be performed on a single day. If you participate in more than one scan, they will normally occur within a year of your first scan, unless it is a yearly follow-up.

The number of people expected to take part in this research study at this site between May 2015 and April 2020 is 500.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved.

Not all procedures described below will necessarily be included in the study for each participant. Everything you will be asked to do will be explained in detail to you prior to your giving consent (signing this form) by a member of the study personnel. All the procedures, how long they will take, and in what order will be explained. You will be able to ask any questions you may have,

A typical visit includes a discussion of the study with a member of study personnel and review of safety considerations for the study. Following that, simple tests such as blood and urine tests are performed if required, before undertaking an imaging study.

Your clinical history will be collected prior to imaging, in some cases you may be asked to fill out an in-depth medical history questionnaire related to your risk factors. In addition, some of your clinical history may be used to assess your risk factors that can be compared to the results of the imaging studies.

The following tests may be included in this study:
1) Blood test, or finger stick test for checking blood sugar or kidney function and urine collection to check your pregnancy status to make sure the imaging tests are safe for you.
2) MRI imaging (taking pictures of the heart and/or vessels and/or brain or other part of the body) without a special contrast agent
3) MRI with a special contrast agent (optional)
4) PET/CT imaging (taking pictures of the heart and/or vessels or another part of the body)
5) PET/MR with or without standalone CT

You will be able to participate in this study if you consent to have at least either an MRI without contrast and/or a PET/CT and/or a PET/MR. Each test will be described individually and you will be asked to decide about each.

Women who are or may be pregnant cannot undergo any MR or PET imaging, as the scans and dyes used may be harmful to the unborn child. Any woman of childbearing potential will be asked to take a urine pregnancy test before she has each scan. If the pregnancy test is negative, she will be able to participate in the study. Women who have had a complete hysterectomy or who are older than 51 and whose last menstrual period was more than 12 months ago may waive the need for a urine pregnancy test.

A description of each test follows.

Non-imaging tests

1. Blood tests (approximately three tablespoons) or finger stick tests may be taken to test for blood markers related to cardiovascular disease, e.g. for cholesterol levels, a complete blood count, cell analysis (e.g. flow cytometry), gene expression analysis, and blood measures of inflammation such as CRP,MMP9, VCAM1, 1CAM1 and CD40 unless they have already been done in the last three months. If you consent to undergo MRI with contrast agent, a blood test may be performed before imaging to test your kidney function as detailed above. If possible a finger-stick test will be performed instead of a blood test to check your kidney function.
2. A finger-stick test will be performed to check your kidney function if you decide to undergo MRI with contrast agent. In case this is not possible, a blood test will be performed instead.
3. If you are a diabetic, you may also be asked to give a urine sample in addition to the blood test, to determine the presence or absence of protein leakage from your kidneys.
4. If you agree to participate in a PET scan you may be required to have a blood test at the time of imaging to check your blood sugar level is suitable to have the scan.

Imaging tests

<u>Magnetic Resonance Imaging (MRI)</u>

Magnetic resonance imaging (MRI) is a safe imaging method that uses powerful magnets to create pictures of the inside of the body, but does not use X-rays. However, MRI cannot be used for some people who have certain types of metal in their body, including pacemakers, metal plates, any eye injuries involving a metallic fragment (e.g. metallic shavings) and other metallic implants. You will be given a questionnaire before your scan to determine if it is safe for you to have an MRI. Also you need to complete a brief healthcare questionnaire. These two questionnaires will take approximately 5-10 minutes to complete. Help will be readily provided should you have any questions.

For women:

Women who are or may be pregnant must not take part in this study, as the scans used may be harmful to the unborn child. Any woman of childbearing potential will be asked to take a urine pregnancy test before she has each scan. If the pregnancy test is negative, she will be able to participate in the study. Women who have had a complete hysterectomy or who are older than 51 and whose last menstrual period was more than 12 months ago may waive the need for a urine pregnancy test.

You will be asked to put on a hospital gown before your MRI scan. Jewelry, credit cards, watches and other magnetic materials must be removed, and will be placed in a personal locker that will be locked. Items are put into a locker to protect them from the MRI, which may erase credit cards, alter your watch or may cause injuries if in contact with the machine.

The MRI scanner looks like a long tube with a table attached to it. You will lie down on the table. The technologist will help position you for the exam. The technologist may put three one-inch pads on your chest over the area of your heart, or a pulse monitor on your finger. This is so we can monitor your heartbeat and breathing patterns during the scan. The technologist will also place a device called a 'coil' on you. The coil is a soft, light-weight pad covered with a foam-like fabric. The coil acts like an antenna, and helps the MRI machine create better pictures of the arteries. While the exam is in progress, the technologist will be in a different room. However, the technologist will be able to see you at all times through a large window, and you will be able to talk with him or her through an intercom.

When the exam begins, the table on which you are lying on will slowly move into the MRI scanner. You will hear some loud knocking and clanging noises, which some people may find unpleasant, which are normal sounds the MRI scanner makes. You will be offered earplugs to wear. Some people may feel closed in as they enter the MRI scanner. If you feel uncomfortable, please tell the technologist and you will not be able to take part in the study.

It is very important that you lie as still as possible during the exam because movement may cause the pictures to be fuzzy and unclear. You will be in the scanner for 60 to 90 minutes. If you are claustrophobic in an MRI you will not be able to take part in the study.

<u>Magnetic Resonance Imaging (MRI) with contrast</u>

The study doctor would like to request your consent to use a dye called gadolinium (for example gadopentatedimeglumine, Magnevist, or gadofosvesettrisodium, Ablavar) during the scan. This is often called 'contrast'. The dye is given through a small tube in a blood vessel (vein) in the back of the

hand or forearm. This tube will be inserted by one of the nurses or a certified technologist. Inserting the tube into your vein may cause minimal discomfort. If you do not want this to be done, you can still take part in the study but not have the injection of dye. Gadolinium is considered a safe, FDA (Food and Drug Administration)-approved contrast agent used routinely in MRI scanning to make objects brighter in the scan. The FDA has recently issued a warning about contrast agents which contain gadolinium, paying particular attention to some subjects who have acute or chronic kidney disease. Any subject who is considering having an MRI with contrast will be provided with a blood test to measure their serum creatinine levels and calculate the GFR (a measure kidney function) to determine that it is safe to have the MRI contrast agent. If a patient has a recent test result (within 2 weeks) from an appropriate source such as their Mount SInai physician, that will be accepted.. The creatinine is a waste product in your blood that comes from muscle activity. It is normally removed from your blood by your kidneys, but when kidney function slows down, the creatinine level rises. We will use the results of your serum (from either a finger-stick or blood draw) creatinine test to calculate your glomerular filtration rate (GFR). The GFR tells us your kidney function. Any subject who has a GFR of less than 40mL/min/1.73m^2 will be considered to have kidney disease and will not be able to be scheduled for MRI with contrast. If your test shows your GFR level is too low, one of the study personnel or the nurse present will tell you of your kidney test result. You may then wish to consult with your own doctor.

If your meet these criteria, you will be given a standard clinical dose, approximately 20 to 40 mL (or between 1 to 3 tablespoons) of contrast and then scanned. At the end of each scan, the tube in your vein will be removed.

For women:

Women who are or may be pregnant, or are breastfeeding, must not take part in this study, as the scans and dyes used may be harmful to the unborn child. Any woman of childbearing potential will be asked to take a urine pregnancy test before she has each scan. If the pregnancy test is negative, she will be able to participate in the study. Women who have had a complete hysterectomy or who are older than 51 and whose last menstrual period was more than 12 months ago may waive the need for a urine pregnancy test.

If you are eligible to have an MRI with contrast and you consented to it during of your first MRI visit, you may consent to a second MRI with contrast. All subjects that do not qualify for contrast agent injection during the first visit (GFR less than 40mL/min/1.73m^2), will not be asked participate in this portion of the study. If you choose to have a second MRI with contrast, the procedure for contrast agent injection will be the same as described for the first visit.

<u>Positron Emission Tomography – Magnetic Resonance Imaging (PET/MR)</u>

Positron Emission Tomography – Magnetic Resonance Imaging (PET/MR) is a new technology that combines a positron emission tomography scanner (PET) and a magnetic resonance imaging scanner

(MRI). This scanner has been developed to reduce the radioactive dose given to the patients by replacing the CT from a PET/CT scanner with a non-radiation technology such as MRI. PET is a non-invasive imaging technology that produces very accurate functional images of the body organs and tissues, and in this case, your arteries. To produce these images, the PET camera detects the energy released by a dye. The dye contains a small amount of radioactivity, which will be injected into a small tube, which will be placed in a vein in your forearm. The dye will be randomly selected between either FDG, fluorodeoxyglucose, NaF, sodium fluoride. The different dyes may be combined but the PET technologist will adjust the doses so that the total amount of radiation you are exposed to will stay the same. The dyes FDG, NaF, are FDA-approved and widely used in hospital PET scans and there is no additional risk in mixing them. Other studies have used this mixture and shown no risk. This tube will be inserted by one of the PET/MR technicians or nurses and causes minimal discomfort. The scan will begin approximately 1 hour later; there is a comfortable lounge to wait in during this time. You will lie on the table in the scanner for about 1 hour inside the PET/MR scanner (see Magnetic Resonance Imaging paragraph above) covered by a blanket with your head resting on a soft cushion. Approximately three tablespoons of blood will be taken from the same tube in your arm to measure your blood sugar level. If you are not diabetic, you may be asked to take some glucose prior to injection of the dye. This will either be a bottle of sugary drink or chewable glucose tablets similar to those available in regular drug stores.

If you are eligible to have a PET/MR and you consented to it during of your first visit, you may consent to either i) a second PET/MR or ii) a PET/CT scan, or iii) a series of up to four PET/MR studies, or iv) follow up PET/MR studies as often as one scan every 3 months. In the case of four PET/MR scans (option iii), the radiation dose will be reduced for each scan so that the total dose is equivalent to two regular PET/MR scans. For follow up PET/MR studies (option iv) you will not be able to participate for the full 5 years of the study. NO PARTICIPANT WILL BE ABLE TO HAVE MORE THAN 10 PET SCANS IN THE FULL DURATION OF THE STUDY. All subjects that cannot undergo PET/MR during the first visit, will not be asked participate in this portion of the study. If you choose to have a second PET/MR, the procedure will be the same as described for the first visit.

<u>Positron Emission Tomography – Computed Tomography (PET/CT)</u>

For this scan, you will be asked to wear a gown, then to lie on the table in the scanner for about 30 minutes covered by a blanket with your head resting on a soft cushion. The technologist will put three one-inch pads on your chest over the area of your heart to electrically trace your heartbeat. A dye containing a small amount of radioactivity (either FDG, fluorodeoxyglucose, , NaF, sodium fluoride,), which will be injected into a small tube, which will be placed in a vein in your forearm. The different dyes may be combined but the PET technologist will adjust the doses so that the total amount of radiation you are exposed to will stay the same. The dyes FDG, NaF are FDA-approved and widely used in hospital PET scans and there is no additional risk in mixing them. Other studies have used this mixture and shown no risk. This tube will be inserted by one of the PET/CT technicians or nurses and causes minimal discomfort. The scan will begin approximately 1 hour later; there is a comfortable lounge to wait in during this time. You will lie on the table in the scanner for about 30 minutes covered

by a blanket with your head resting on a soft cushion. The scan is almost silent, and you will be required to lie as still as possible. The bed will slowly move through the scanner, which will take pictures of your blood vessels. Approximately three tablespoons of blood will be taken from the same tube in your arm to measure your blood sugar level.

If you are eligible to have a PET/CT and you consented to it during of your first visit, you may consent to a PET/MR scan. However, you cannot undergo a second PET/MR if you consented to both PET/CT and PET/MR during your first visit.

For women:

Women who are or may be pregnant, or are breastfeeding, must not take part in the PET component of this study, as the radioactive dyes used may be harmful to the unborn child. Any woman of childbearing potential will be asked to take a urine pregnancy test before she has each scan. If the pregnancy test is negative, she will be able to participate in the study. Women who have had a complete hysterectomy or who are older than 51 and whose last menstrual period was more than 12 months ago may waive the need for a urine pregnancy test.

For men:

Since you are participating in a study that involves a radioactive dye with potential risks to a developing fetus, it is recommended that you use a condom and not father a child or donate sperm for up to 12 hours after injection of the radioactive dye.

CT

Computed tomography (CT) is a technique very similar to the X-rays to obtain 3D images of your neck, from the external auditory meatus to the aortic arch. A low dose CT scan will be performed to allow attenuation correction for the PET images on the PET/MR study.

For women:

Women who are or may be pregnant, or are breastfeeding, must not take part in this study, as the scans used may be harmful to the unborn child. Any woman of childbearing potential will be asked to take a urine pregnancy test before she has each scan. If the pregnancy test is negative, she will be able to participate in the study. Women who have had a complete hysterectomy or who are older than 51 and whose last menstrual period was more than 12 months ago may waive the need for a urine pregnancy test.

Because of the radiation exposure involved in PET and CT imaging you should inform your physician(s) that you have participated in this research study.

All imaging scans will be read by a qualified radiologist. Should we find any clinically significant findings on any of your scans that could be important to your health care, we will contact you and/or your treating physician.

Please mark the tests that you are consenting to and put your initial below

MRI (1)	□		
MRI (2)	□		
MRI (3)	□		
PET/CT	□		
PET/MRI (1)	□	with standalone CT	□
PET/MRI (2)	□	with standalone CT	□
PET/MRI (up to 4 scans with half-dose)	□		
Follow-up PET/MRI (up to 4 full-dose scans per year but no more than 10 scans in total)	□		

Please note that if you consented to a PET/CT and a PET/MR during your initial visit, you cannot undergo a second PET/MR within one year as part of this study. Also if you consented to undergo two PET/MR scans during your first visit, you cannot undergo a PET/CT scan within one year as part of this study. If you consented to the series of 4 PET/MRI scans at half-dose you cannot undergo any additional PET scans within one year as part of this study. If you consented to more frequent follow up PET/MRI (up to 4 scans per year) you will not be able to participate for 5 years – you will not be able to receive more than 10 PET/MR scans.

Do you consent to the use of MRI contrast agent?	□ Yes □ No
Are you diabetic? Do you consent to taking an oral glucose dose? (You may not check 'yes' if you indicated you are diabetic)	□ Yes □ No □ Yes □ No
Do you consent to yearly follow-up of the tests that you indicated above?	□ Yes □ No
Do you consent to fill out an in-depth medical history questionnaire related to your risk factors?	□ Yes □ No
Have you consented to this study before and are you renewing your consent in order to participate in follow-up PET/MRI? [Please answer this question so that study personnel can accurately track your radiation exposure.]	□ Yes □ No Date of original consent:
For women: to waive a urine pregnancy test complete the following: Have you had a complete hysterectomy? OR: Are you at least 51 years old?	 □ Yes □ No □ Yes □ No

Was your last menstrual period more than 12 months ago?	□ Yes □ No

Please initial here _____

The researchers would like to ask your permission to keep specimens (like blood or carotid endarterectomy specimen) collected from you during this study to use them in future research studies. They would also like to know your wishes about how they might use your specimens in future research studies. You should also know that it is possible that products may someday be developed with the help of your specimens, and there are no plans to share any profits from such products with you.

(1) Will you allow the researchers to store your specimens to use in future research studies?
Yes_____ No_____ If no, please stop here. If yes, please continue to the next question.

(2) The researchers can keep your specimens stored in one of two different ways: one way will store your specimens in a way that it is linked to your identity (through the use of a code that can indicate the information came from you personally) and the other way will store your specimens anonymously (no one will know who the information is from). It will not be stored both ways, so you must choose one of these two options. Please note that if you choose to have your specimens stored anonymously, you will not be able to change your mind to ask for your specimens to be destroyed at a future date.
How would you like your specimens stored? Please initial **ONE** choice:

I would like my specimens stored with a link to my identity_____
I would like my specimens stored anonymously _____

(3) Do you give the researchers permission to **contact you** in the future to collect additional information about you, discuss how your specimens might be used, or to discuss possible participation in another research project? Please initial your choice:
Yes_____ No_____

(4) Do you give the researchers permission to keep the specimens indefinitely and use them for future studies that are **directly related** to the purpose of the current study? Please initial your choice:
Yes_____ No_____

(5) Do you give the researchers permission to keep the specimens indefinitely and use them for future studies that are **not related** to the purpose of the current study (for example, a different area of research)? Please initial your choice:
Yes_____ No_____

(a) If the future research in a different area can be done without having to know that the specimens came from you personally, that will be done.

(b) If the future research in a different area requires that it is known specifically who the specimens came from, then one of the following will be done:

(i) If you allowed the researchers to contact you in the future, they will be able to contact you to explain why your specimen is needed and what will be done with it. Your permission will be asked to use your specimens in that research project.

(ii) If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical, for example, because you have moved, your specimens may still be used. Either all links to your identity will be removed from the specimens, or an Institutional Review Board will be asked for permission to use the specimens linked to your identity. The Institutional Review Board (IRB) is a committee of doctors and scientists and non-scientists and people not associated with this hospital or medical school whose job it is to protect people who participate in research. The IRB can give permission for researchers to use and share health information connected to specimens that are linked to people's identities, but only if it determines that doing this will not be more than a minimal risk to people or their privacy.

(6) Do you give permission to have portions of the specimens **given to other researchers** at Mount Sinai or other institutions for use in research that is either related or not related to the purpose of this study? Please initial your choice:

Yes_____ No_____

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things: attending the study visits that you consented to, and complying with dietary instructions if any.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

If you agree to take part in this research study, we will pay you $75 per scan for your time and effort. Typically, this study requires two scans, however, if you prefer it may be possible to complete various components in separate visits (this will be determined with you by study personnel). If you take part in the maximum allowed 5 scans per year you will be reimbursed $375 per year. If you also take part in the maximum 5 scans per year and also participate for the maximum allowed 5 years, you will be reimbursed a total of $1,875 over the duration of the study. You will be paid by either check or cash. A check will be mailed directly to you approximately one month after you have completed the study. Checks require some time to be prepared and will be given to you as available.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally this reporting would take place if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

It is possible that the results of these scans might lead to further evaluation, tests and/or other procedures. All other costs that may occur because of your participation in this study will be paid for by you or your insurance company.

POSSIBLE BENEFITS:

It is important to know that you will not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be providing your doctor with more information about your arteries and/or your heart. If you have atherosclerosis or some cardiomyopathy, the MRI and CT examinations have the potential to help study the extent of your disease, and provide to your doctor with more information about your arteries and heart in general. We also hope to provide a better understanding of atherosclerotic disease and possibly help future patients.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

Women who are or may be pregnant, or breastfeeding may not take part in this study and before their scan they must take a urine pregnancy test, as the scans and dyes used may be harmful to the unborn child. Any woman of childbearing age who thinks they could possibly be pregnant must have a negative urine pregnancy test before each scan in order to take part in the study. Women who have had a complete hysterectomy or who are older than 51 and whose last menstrual period was more than 12 months ago may waive the need for a urine pregnancy test.

You should not become pregnant or father a baby for up to 12 hours after injection of the radioactive dye involved in the PET study. Please see the Description of What's Involved section of this document.

1. **MRI**: The MRI machine is an oversize magnet that is always on. It is dangerous to approach the machine if you are carrying any kind of metallic or magnetic object. You will be escorted by a technician or one of the investigators after all safety issues are assured.

Some people may be uncomfortable in an MRI scanner as it involves being in a small space. Therefore, if you suffer from claustrophobia (fear of enclosed spaces), you are encouraged not to participate. MRI can be noisy and uncomfortable and carries the common risks to hearing of overly-loud noises. You will be provided ear plugs and offered additional ear defenders to eliminate this risk. Please tell the technologist if you have any concerns. In this study, MRI will be performed in the usual

way, without any medications to make you relaxed, but you will be scanned during the performance of simple activities. These activities, which may include seeing flashing words and numbers or images such as human faces expressing happy, neutral or angry emotions are part of this research study. You will receive instructions on how to perform the activity before the MRI begins.

2. **MRI with contrast**: Gadolinium (MRI dye) is routinely used in medical imaging. As described in the MRI safety literature, it is a substance that is not normally absorbed into the tissues of the body. Once it is injected, it will stay in the blood stream and will be eliminated a few hours later in the urine. Some patients very rarely have a reaction to this dye, which may be body itching, nausea, breathing problems, vomiting, or a metallic taste. These reactions are very rare and usually occur in people who already have severe lung disease. A safety questionnaire will be given to you before the injection to make sure you are safe to have the dye injection. If you are not a candidate for this dye, the MRI scan can be done without it. A recent FDA warning has been issued that states subjects with kidney problems must not be given contrast because it may lead to a debilitating and potential fatal disease that involves the skin, muscles and internal organs. Patients with kidney disease can develop skin thickening that may prevent bending and extending joints, resulting in decreased mobility of joints. In addition, patients may experience scarring that has spread to other parts of the body such as the diaphragm, muscles in the thigh and lower abdomen, and the interior areas of lung. The chances of developing nephrogenic systemic fibrosis (NSF) is extremely low in individuals with normal kidney function. There is a slight chance of an allergic reaction, from the contrast which has a less than one in 300,000 chance that this will be severe. There is no increased risk to the amount of contrast that is injected over the two MRI sessions.

3. **PET/CT and PET/MR**: FDG, , NaF, , the contrasts used for PET/CT and PET/MR, are respectively a radioactive sugar, , a radioactive salt,. Most of these tracers is excreted in the urine, while the rest breaks down in the body by radioactive decay. As a result, no significant radioactivity remains in the body after about ten hours. We do not expect any side effects at all either during or after the scan. Subjects who receive a FDG, NaF, injection as part of the study *should not be the primary caregivers for small children or be in close prolonged physical proximity to women of childbearing age who might be or are pregnant, for up to 10 hours after imaging*.

Both PET/MRI and PET/CT are known to provide information on the presence of local inflammatory activity but PET/MRI delivers slightly less ionizing radiation to the patients than PET/CT. PET/MRI is still an investigational. For this reason, PET/MRI results will be compared with PET/CT when available.

4. CT Examination

CT scans use x-rays to produce a 3D image. A low dose CT scan would be used to correct the PET images for attenuation correction and to fully validate the PET/MR imaging. The low-dose CT scan acquisition last less than a minute. CT is widely used in oncology and cardiology.

5. Ionizing Radiation Risks

Radiation is measured in units called milliSieverts (mSv.). Below is a table showing the radiation exposure from each test involved in the study:

Test	Exposure
One PET test	7 mSv
One low dose CT	0.7 mSv
One PET/CT test	7.7 mSv
One PET/MRI	7 mSv (MRI emits no ionizing radiation)

This research study includes exposure to radiation from x-rays or gamma rays. This radiation exposure is for research purposes only, and is in addition to any radiation needed for your medical care. X-rays and gamma rays from natural or medical sources can damage the genetic material (DNA) in your cells. At low doses, the body is usually able to repair the damage. Radiation risk is believed to be related to the total lifetime exposure. You should think about your own history of radiation exposure from tests (like x-rays or CT scans) in deciding about the radiation in this study. If you have questions about the total amount of radiation you will be receiving, you should ask your doctor.

Subjects who receive a FDG, , NaF, injection as part of the study ***should not be the primary caregivers for small children or be in close prolonged physical proximity to women of childbearing age who might be or are pregnant, for up to 10 hours after imaging***

Depending upon the types of imaging that you undergo, the maximum estimated radiation exposure that you will get for this research study will be 77.0 mSv over the length of the study (an mSv is a unit of absorbed radiation). The greatest annual exposure (15.4 mSv) will be at least in year 1, but also possibly in subsequent years if you choose to undergo the same imaging in each of those years. If you choose to undergo more frequent follow up imaging the maximum dose in 1 year may be 30.8 mSv but the total radiation exposure in the study will not exceed 77 mSv. This effective radiation dose exceeds the 6.2 mSv that the average person in the United States gets each year from both natural sources like the sun, outer space, air, food and soil, as well as from medical procedures. It is less than the 50 mSv of radiation that is allowed each year for people who are exposed to radiation in their jobs.

6. **Blood drawing**: The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw. Care will be taken to avoid these possible risks.

There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk. Your images will be stored in locked computer that is password protected. A locked filing cabinet will be used to store consents and any other associated paperwork. Both the filing cabinet and computer are located in the Translational and Molecular Imaging Institute at Mount Sinai. The data will be stored for seven years. The principal investigator and the research team will have access to the data. Encrypted patient identifiers will be associated to the data. To ensure confidentiality, a database in the password protected computer will provide the link to the patient identification number and the patient's name. Tissue specimens collected from carotid

endarterectomy and carotid stenting will be used for histological analysis. Histological analysis of tissue specimens will be compared with imaging findings to aid in the validation of the imaging methodologies used in this study. Specimens will be stored anonymously (no one will know who the information is from). You may be contacted after imaging to collect additional information about you, discuss how your specimens might be used, or to discuss possible participation in another research project. We may to keep the specimens indefinitely and use them for future studies that are directly or not directly related to the purpose of the current study. In the future we may give the specimens to other researchers at Mount Sinai or other institutions for use in research that is either related or not related to the purpose of this study.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to you or your insurance in the ordinary manner and you will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at Mount Sinai or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff. If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the investigator can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

If you have given permission for specimens to be stored, they may not be removed from the research study database and will continue to be used to complete the research analysis.

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study

may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the office of the research team and/or the Principal Investigator at phone number 212-824-8452.

If you experience an emergency during your participation in this research, contact:

1. If you are at home, call 911 or your Primary Care Physician or go to the nearest Emergency Room;
2. Alert the research personnel if you are experiencing an emergency during the procedure

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our

website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

One or more researchers has a financial interest that could be affected by the outcome of this research study.

Dr. Claudia Calcagno-Mani and Dr. Venkatesh Mani (Co-investigators in this study) are named inventors on an issue patent relating to Dynamic Contrast Enhanced Magnetic Resonance Imaging.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be disclosed (shared) with others?

As part of this research project, the researchers will collect your name, address, telephone/fax number, dates directly related to you (birth, admission, discharge, date of death, etc.), e-mail/internet protocol (IP) addresses or web universal resource locators (URL's), social security number, medical records number. The researchers will also get information from your medical record from Mount Sinai Hospital, your private doctor, or health care provider and all other health care institutions that keep your Medical information

During the study the researchers may gather information by:

- Taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- Doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- Completing the tests, procedures, questionnaires and interviews explained in the description section of this consent. This includes blood tests, including the ones that are indicators of disease or risk factors related to your fat deposits. These include Total Cholesterol, cholesterol profile, glycohemoglobin (a marker for diabetes), fasting glucose (Blood sugar levels), pregnancy test (if applicable) and urine analysis.
- Other procedures that you may have done in the past and data present in your Medical Records. These procedures include, but are not limited to computer tomography (CT), X-Ray Angiography, ultrasound, previous MRI studies, tissue analysis and blood results.
- The list of your current and past medications

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- Other collaborating research center(s) and their associated research/clinical staff who are working with the investigators on this project: Hospital for Special Surgery, Mount SInai St Lukes, and other sites available on request.
- The sponsoring government agency and/or their representative who need to confirm the accuracy of the results submitted to the government or the use of government funds: Icahn School of Medicine at Mount Sinai
- The United States Food and Drug Administration
- The United States Department of Health and Human Services and the Office of Human Research Protection.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving

the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information? Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your protected health information.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of

medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Signature Block for Capable Adult

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

DO NOT SIGN THIS FORM AFTER THIS DATE → **12/31/2019**

Signature of subject	Date
Printed name of subject	Time

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent	Date
Printed name of person obtaining consent	Time

Witness Section: For use when a witness is required to observe the consent process,, document below (for example, subject is illiterate or visually impaired, or this accompanies a short form consent):

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	*Date*
Printed name of person witnessing consent process	Time