Noninvasive Assessment of Abdominal Aortic Aneurysm Wall Structural Integrity and Inflammation as Predictors of Expansion and/or Rupture

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INFORMED CONSENT DOCUMENT

Project Title: Noninvasive Assessment of Abdominal Aortic Aneurysm (AAA) Wall Structural Integrity and Inflammation as Predictors of Expansion and/or Rupture

Principal Investigator: **Sean English, M.D.**

Research Team Contact: **Julie Wilson, RN** **314-747-7828**
Ashley Burgess, RN, BSN **314-362-6257**

This consent form describes the research study and helps you decide if you want to participate. It provides important information about what you will be asked to do during the study, about the risks and benefits of the study, and about your rights and responsibilities as a research participant. By signing this form, you are agreeing to participate in this study.

- You should read and understand the information in this document including the procedures, risks, and potential benefits.
- If you have questions about anything in this form, you should ask the research team for more information before you agree to participate.
- You may also wish to talk to your family or friends about your participation in this study.
- Do not agree to participate in this study unless the research team has answered your questions and you decide that you want to be part of this study.

WHAT IS THE PURPOSE OF THIS STUDY?

This is a research study. We invite you to participate in this research study because you either have a known abdominal aortic aneurysm (AAA) or because you do not have an AAA (control group).

The aorta serves as the main artery to supply blood flow to the body. It is approximately the size of a garden hose. Due to the effects of high blood pressure (hypertension), atherosclerosis (hardening of the arteries), and tobacco use, the aorta may widen and enlarge to form an aneurysm. An abdominal aortic aneurysm (AAA) is a dilation (enlargement) or ballooning out of a section of blood vessel caused by disease or weakness in the wall of the aorta below the level of the kidney arteries. As an AAA dilates and increases in size, rupture of the AAA may occur. AAA rupture carries a significant risk of death.

Currently, aortic size is the primary factor used to assess aortic rupture risk. There are other imaging procedures (imaging modalities) that are being used and developed to assess AAA rupture risk. Finite element analysis (FEA) is a way to study the mechanical properties of the aortic wall, including areas of stress and strength that are used to calculate rupture risk. Positron Emission Tomography (PET) utilizes glucose (a form of sugar) labeled with a radioactivity to look at the metabolic activity and inflammation in the aortic wall.

The purpose of this research study is to further study, through FEA, changes that occur in the mechanical properties of the aortic wall. We would like to compare two radiotracers, ^{18}F-FDG and ^{11}C-PBR28 to determine if one provides more useful and reliable information about inflammation. 18F-FDG and 11C-PBR28 are radioactive drugs that will be used for imaging during your PET-CT scan. We

would also like to compare the results describing the mechanical properties of the AAA wall to the degree of inflammation in that wall as determined by PET-CT imaging to define new and better predictors of AAA growth and/or rupture.

The radioactive tracers that are used in this study are ^{18}F-fludeoxyglucose (FDG) and ^{11}C-PBR28 (PBR which stands for Peripheral Benzodiazepine Receptor. ^{11}C-PBR28 is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration. FDG is an approved drug by the FDA, however in this study it is considered investigational

WHAT WILL HAPPEN DURING THIS STUDY?

Screening Procedures:

If you agree to participate in this study, you will be asked to have a blood draw, approximately 1-2 teaspoons of blood, taken from a vein in your arm, so that we can perform a genetic test. This genetic test will look at genes and proteins that may be expressed more frequently in AAA. Depending on the results of the genetic test your study doctor will determine whether you will be eligible to proceed to the PET-CT imaging portion of the study. The study team will communicate to you a plan following the genetic test (proceed to scanning or ending participation). You will not be made aware of the results of the genotyping.

If you go on to the scanning portion of the study, we will ask you some standard questions to make sure that it is safe for you to undergo a PET-CT scan. If you have not had a renal function blood test performed within the past 90 days, we will draw approximately 2 teaspoons of blood for a creatinine test. We will also ask for your permission to use a contrast dye for the CT portion of the PET-CT scan. The contrast agent helps us see the blood circulating (moving around) in your body and blood vessels. If you agree, we will ask you some additional questions to see if you are eligible to receive the contrast dye.

Imaging will be performed using a combined PET-CT scanner to take pictures of your body. A PET/CT (Positron Emission Tomography (PET) combined with Computed Tomography (CT) imaging camera. PET scanners allow us to image the function of different cells and organs in the body after you are injected with a radioactive tracer. The CT scan (computed tomography) is an x-ray scanner that images the anatomy (size or structure) of the body giving us detailed images such as pictures of the aorta, other blood vessels, and surrounding tissues. The PET-CT scanner is a large tube in the shape of a donut with a padded imaging table in the middle of the machine that records images of your body after the injection of the iodinated contrast and radioactive tracers. A radioactive tracer is often a naturally occurring substance that contains a small amount of radioactivity so pictures can be taken of your abdomen and pelvis.

You will be given an injection of a small amount of a radioactive drug/tracer (a chemical similar to sugar which is called FDG) into a vein in your arm. The amount of radiation is very small, no more than what you would have during a normal x-ray. It only stays in your body for a few hours. The FDG will travel to particular parts of your body where glucose is used for energy, such as the aorta.

PET scanning can make pictures of structures inside the body because the tracer "lights up" on the pictures. This shows us details of the aorta, other blood vessels, and surrounding tissues. The radioactive material breaks down and leaves your body gradually through the urine. It takes about 1 day for the radioactive material to exit your body completely.

Since the effects of radiation can be cumulative, it is important to know about your past research related radiation exposure. If you have participated in other research studies in the past 12 months that have involved radiation exposure, please inform the investigators or study staff. If it is determined that your prior radiation exposure exceeds our current guidelines, it is possible that you will not be allowed to participate in this study.

Please place your initials in the blank next to 'I have' or 'have not' for each of the questions below:

I have _____have not _____participated in research studies involving radiation exposure within the last 12 months.

PET-CT with Contrast CT Angiography imaging:

If you are to proceed to the imaging portion of the study, we will ask that you undergo PET-CT imaging that will last approximately 3 hours. On the day of your imaging scan, you will be asked to come to the Center for Clinical Imaging Research Facility (CCIR) located within the Barnes-Jewish Hospital complex. Wear comfortable clothing and bring an updated medication list.

Your imaging visit will have the following procedures:

- If you are a woman who can become pregnant, we will perform a urine or blood pregnancy test (blood test, approximately 2 teaspoons of blood) prior to performing the PET-CT scan. Pregnant and breastfeeding women may not take part in this study.
- We will require that you fast for approximately 12-16 hours prior to your PET-CT scan. This means you will not eat solid food during that 12-16-hour period. You may drink water and should drink at least two or three glasses of water during this time.
- We will also ask that you refrain from heavy exercise for 24 hours prior to the study.
- You may need to change into a hospital gown if you have anything on your body that contains metal, such as jewelry, piercings, or zippers.
- You will have two (2) intravenous (IV) catheters placed in the veins of your arms, usually one IV in each arm for the purpose of radioactive tracer injections and the other for contrast agent injection or to draw blood samples. An IV catheter is a thin, flexible tube that is placed in a vein with a needle.
- We will also check your blood sugar using a drop of blood from your IV line or by a finger stick to make sure that it is low enough for us to get an accurate picture of inside your body.
- Vital signs (blood pressure and heart rate) will be obtained prior to imaging. Additional vital signs may be taken during the imaging scans.

You will be positioned on the PET-CT imaging table lying flat with your arms resting above your head

or across your chest out of the field of view. You will be made to feel as comfortable as possible. We will ask you to lie still during the imaging scan of your abdomen and pelvis. The imaging table will slowly move you into the scanner. You will be given the radiotracer ^{11}C-PBR28 through your IV followed by up to 40-minutes of PET imaging. Next, you will be given FDG tracer and then you will remain in the scanner and be given an iodine contrast material (dye) through your IV followed by approximately 10 minutes of CT imaging. Upon completion of the CT imaging scan, you will be removed from the scanner and escorted to the bathroom and encouraged to empty your bladder. Next, you will be placed in a quiet room to rest in a reclining chair before your next imaging scan. You will not be able to eat during this time, but you may drink water. Prior to the next imaging scan, you will again be escorted to the bathroom and encouraged to empty your bladder before placing you back in the in the PET/CT scanner. You will again be positioned on the imaging table lying flat with your arms as they were for the first scan. The imaging table will slowly move you into the scanner and you will have 20 minutes of PET imaging performed.

After the scan is completed:
When you have completed the study, we will remove the IV catheters and place bandages the places on your arms. You may feel tired after the imaging scans because you have been fasting for several hours. We will offer you a snack while you rest before leaving the imaging facility. You should drink plenty of water to help flush the radioactive material out of your body. This is a natural process for the body to rid itself of the radioactivity through your kidneys.

Will you save my samples or research data to use in future research studies?
As part of this study, we are obtaining blood samples and PET-CT scans from you. We would like to use the PET-CT scans and data obtained from those scans for studies going on right now as well as studies that are conducted in the future. These studies may provide additional information that will be helpful in understanding vascular disease, or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the U.S. Food and Drug Administration. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur. By allowing us to use your PET-CT scan results you give up any property rights you may have in these scans.

We will share your PET-CT scans with other researchers. They may be doing research in areas similar to this research or in other unrelated areas. These researchers may be at Washington University, at other research centers and institutions, or industry sponsors of research. We may also share your research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

If you change your mind and do not want us to store and use your PET-CT scans for future research you should contact the research team member identified at the top of this document. The PET-CT scans will no longer be used for research purposes. However, if some research with your PET-CT scans has already been completed, the information from that research may still be used. Also, if the PET-CT scans have been shared with other researchers it might not be possible to withdraw the PET-CT scans to the extent it has been shared.

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 30 people will take part in this study conducted by investigators at Washington University. All will have a blood sample drawn for genetic testing and those that qualify will have PET-CT imaging. Approximately twenty-four (24) people will be enrolled into the imaging portion of the study. Twelve (18) subjects will have a known AAA and six (6) will be free of any known AAA (control group).

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your involvement will last until your imaging has been completed. If your study doctor notifies you that your genetic testing did not qualify you to continue with the imaging portion of the study, then your participation will end at that time.

WHAT ARE THE RISKS OF THIS STUDY?

You may experience one or more of the risks indicated below from being in this study. In addition to these, there may be other unknown risks or risks that we did not anticipate, associated with being in this study.

Some risks described in this consent document, if severe, may cause death.

Risks associated with the IV:
Placing an IV catheter into your arm may cause some pain, discomfort, bruising, bleeding, swelling, and redness in that area. There is a slight risk of infection which can be treated, temporary loss of pulse at the wrist, and fainting. You may have a bruise, feel pain, or be uncomfortable for 2-3 days after the IV catheter is removed. Rarely, an infection may occur at this site, and if the infection does occur, it will be treated appropriately.

Risks associated with the blood draw may include:
Likely:
Mild
Pain at the needle stick site

Less Likely / Less Common
Mild
The blood draw may cause bleeding or bruising.

Rare:
Serious
Some people become dizzy or feel faint.
There is also a rare risk of infection.

Risks associated with PET/CT imaging:
Likely: Lying still in the scanner may produce some stiffness. Study staff will be nearby to stop the study in case you become too uncomfortable.

Less likely: You may experience aching in your joints and muscles from lying very still. This research may produce some anxiety and discomfort.

Rare: A small fraction of participants experience claustrophobia (anxiety due to being restrained or in a confined area) while some experience dizziness or feel faint. If you experience any of these symptoms and do not wish to continue for any reason, the study will be stopped immediately.

Medical Devices: There is a rare risk of malfunction of worn or implanted electronic medical devices with MRI and CT scanning. If you wear or have an electronic medical device implanted, such as an insulin pump, you will be asked to tell the study investigator and research staff.

Risks of Unexpected Findings:
We are doing the PET-CT scan in the study to answer research questions, not as part of your medical care. The information created by this study will not usually become part of your hospital record. This PET-CT scan is not the same as the one that your own doctor would order. It may or may not show problems that would be found on standard PET or CT scans.

The imaging performed for this study is for research purposes only. We will only evaluate the infrarenal abdominal aorta. Other organs and anatomic structures in the field of view will be evaluated by a radiologist on the study team for incidental findings. You will be made aware of the results of incidental findings. The results of this study may be incorporated in the decision making regarding your aortic pathology; however, your ultimate management will be dictated by current standards of care.

Risks associated with ^{11}C-PBR28 and ^{18}F-FDG radiotracers:
Likely: Radioactive tracers used for PET imaging, ^{11}C-PBR28 and ^{18}F-FDG are not expected to produce any health risks other than those associated with radiation exposure.

Rare: There are no known pharmacological risks or side effects of receiving ^{11}C-PBR28 at the dose you will receive. However, as with any drug, an allergic reaction can occur. Allergic reactions can be mild or serious, and can even result in death in some cases. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat or trouble breathing. If you think you are having an allergic reaction, let us know right away.

^{18}F-fludeoxyglucose (FDG) is a type of radiation emitting product, therefore, may increase the risk of cancer. We use the smallest dose necessary for imaging and ensure safety during injection.

Risks associated with Radiation Exposure:
Please note that this radiation exposure is not necessary for your medical care and is for research purpose only.

Likely: This study will expose you to radiation from the PET-CT imaging scans of your abdomen and pelvis and from the radiotracers ^{11}C-PBR28 and ^{18}F-FDG. The amount of radiation from this, when averaged over your entire body, is approximately 48% of the amount a person who works with radiation is allowed to have in one year. In the event of a failed radiotracer, you may be rescheduled for a make-up imaging visit to complete the study. The maximum amount of radiation from this, when averaged

over your entire body, is approximately 55% of the amount a person who works with radiation is allowed to have in one year. The risk from the radiation exposure in this study is too small to be measured. It is not a big risk when compared with other risks you take every day. If you want to know more about radiation exposure, please see the "Radiation Fact Sheet" at http://hrpo.wustl.edu or ask the study staff for a copy.

Risks associated with the Iodinated Contrast Dye Iopamidol (Routine CT Scan dye):
Rare: Side effects from the contrast dye Iopamidol include:

- Nausea (up to 2 in 100 of people).
- Hives (itchy red bumps on the skin, < 1 in 100 of people)
- Severe allergic reaction, which can be life-threatening (very rarely happens, < 1 in 100,000 people). If you have any signs of allergic reaction, we will treat you immediately.

Allergic reactions can be mild or serious, and can even result in death in some cases. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or trouble breathing. If you think that you are having an allergic reaction, notify the study physician or team member immediately. If you are having trouble breathing, tell us immediately. If you experience any swelling of the face and/or throat, and/or you experience any trouble breathing after you have left the imaging center, call 911 immediately and seek medical assistance.

Radiation Exposure in Women Capable of Becoming Pregnant
You may not participate in this study if you are pregnant or breastfeeding. If you are capable of becoming pregnant, we will perform a pregnancy test before exposing you to research-related radiation. You must tell us if you think there is any chance that you may have become pregnant.

Genetics
There is a federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans and employers with greater than 15 employees to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance or long-term-care insurance.

Breach of Confidentiality
One risk of participating in this study is that confidential information about you may be accidentally disclosed. We will use our best efforts to keep the information about you secure. Please see the section in this consent form titled *"How will you keep my information confidential?"* for more information.

WHAT ARE THE BENEFITS OF THIS STUDY?

You will not benefit from being in this study.

However, we hope that, in the future, other people might benefit from this study because of what we may learn from this study.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You will not have any costs for being in this research study.

You and/or your medical/hospital insurance provider will remain responsible for your regular medical care expenses.

WILL I BE PAID FOR PARTICIPATING?

You will be paid for being in this research study. You will need to provide your social security number (SSN) in order for us to pay you. You may choose to participate without being paid if you do not wish to provide your social security number (SSN) for this purpose. You may also need to provide your address if a check will be mailed to you. It should take approximately 2 – 4 weeks to receive payment for your participation in the study. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

We will pay you $200 for your participation if you complete the study PET-CT scan. If you have to stop the PET-CT scan early for any medical reason or mechanical error, you will still receive the full payment. We will ask you if you are willing to complete the study, if you agree, we will schedule a visit to complete the study at your convenience.

We will provide parking validation if you drive to your study sessions.

WHO IS FUNDING THIS STUDY?

The University and the research team are not receiving payment from other agencies, organizations, or companies to conduct this research study.

WHAT IF I AM INJURED AS A RESULT OF THIS STUDY?

Washington University investigators and staff will try to reduce, control, and treat any complications from this research. If you feel you are injured because of the study, please contact the investigator at (314) 362-3511 and/or the Human Research Protection Office at 1-(800)-438-0445.

Decisions about whether payment for medical treatment for injuries relating to your participation in research will be made by Washington University. If you need to seek medical care for a research-related injury, please notify the investigator as soon as possible.

HOW WILL YOU KEEP MY INFORMATION CONFIDENTIAL?

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people such as those indicated below may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you.

- Government representatives, (including the Office for Human Research Protections) to complete federal or state responsibilities
- The U.S. Food and Drug Administration
- The University of Pittsburgh
- Your primary care physician if a medical condition that needs urgent attention is discovered
- Hospital or University representatives, to complete Hospital or University responsibilities

- The last four digits of your social security number may be used in hospital or University systems to track billing information for research procedures
- Washington University's Institutional Review Board (a committee that oversees the conduct of research involving human participants) and the Human Research Protection Office. The Institutional Review Board has reviewed and approved this study.

To help protect your confidentiality, paper/hard copy records will be stored in a locked suite/locked office by the study team in the Vascular Surgery Office with access limited to only those on the study team. Electronic records for the study will be stored on a secure, password-protected, WU shared network drive with access limited to the study team. FEA will be performed at the University of Pittsburgh. PET-CT scans performed for the study will be copied onto CD, labeled with a study ID only and mailed by a member of the Washington University Study team. No PHI will be provided to University of Pittsburgh and they will not be able to link the FEA or PET-CT back to you. Your blood samples will be labeled with your initials, study number, and date and time of collection. The genetic samples will be drawn by the study team and then transported directly to the vascular surgery laboratory for analysis. These samples will be labeled with your Study ID number, initials, and date/time of collection. Urine pregnancy test (if required) will be performed by the study staff in the CCIR. The pregnancy and genetic samples will be drawn by the study team and then transported directly to a laboratory for analysis.

If we write a report or article about this study or share the study data set with others, we will do so in such a way that you cannot be directly identified.

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.

Are there additional protections for my health information?

Protected Health Information (PHI) is health information that identifies you. PHI is protected by federal law under HIPAA (the Health Insurance Portability and Accountability Act). To take part in this research, you must give the research team permission to use and disclose (share) your PHI for the study as explained in this consent form. The research team will follow state and federal laws and may share your health information with the agencies and people listed under the previous section titled, "How will you keep my information confidential?"

Once your health information is shared with someone outside of the research team, it may no longer be protected by HIPAA.

The research team will only use and share your information as talked about in this form or as permitted or required by law. When possible, the research team will make sure information cannot be linked to you (de-identified). Once information is de-identified, it may be used and shared for other purposes not discussed in this consent form. If you have questions or concerns about your privacy and the use of your PHI, please contact the University's Privacy Officer at 866-747-4975.

Although you will not be allowed to see the study information, you may be given access to your health care records by contacting your health care provider.

If you decide not to sign this form, it will not affect

- your treatment or the care given by your health provider.
- your insurance payment or enrollment in any health plans.
- any benefits to which you are entitled.

However, it will not be possible for you to take part in the study.

If you sign this form:

- You authorize the use of your PHI for this research
- This authorization does not expire.
- You may later change your mind and not let the research team use or share your information (you may revoke your authorization).
  - To revoke your authorization, complete the withdrawal letter, found in the Participant section of the Human Research Protection Office website at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ or you may request that the investigator sends you a copy of the letter.
    - **If you revoke your authorization:**
      - The research team may only use and share information already collected for the study.
      - Your information may still be used and shared as necessary to maintain the integrity of the research, for example, to account for a participant's withdrawal from the research study or for safety reasons.
      - You will not be allowed to continue to participate in the study.

IS BEING IN THIS STUDY VOLUNTARY?

Taking part in this research study is completely voluntary. You may choose not to take part at all. If you decide to be in this study, you may stop participating at any time. Any data that was collected as part of your participation in the study will remain as part of the study records and cannot be removed.

If you decide not to be in this study, or if you stop participating at any time, you won't be penalized or lose any benefits for which you otherwise qualify.

What if I decide to withdraw from the study?

You may withdraw by telling the study team you are no longer interested in participating in the study or you may send a withdrawal letter. A sample withdrawal letter can be found at https://hrpo.wustl.edu/participants/withdrawing-from-a-study/ under Withdrawing from a Research Study.

Will I receive new information about the study while participating?

If we obtain any new information during this study that might affect your willingness to continue participating in the study, we'll promptly provide you with that information.

Can someone else end my participation in this study?

Under certain circumstances, the investigator might decide to end your participation in this research study earlier than planned. This might happen for no reason or because in our judgment it would not be safe for you to continue, because you are or became pregnant, or because funding for the research study has ended.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Dr. Sean English at (314) 362-3511. If you experience a research-related injury, please contact: Dr. Sean English at (314) 362-3511.

If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office at 660 South Euclid Avenue, Campus Box 8089, St. Louis, MO 63110, 1-(800)-438-0445, or email hrpo@wustl.edu. General information about being a research participant can be found on the Human Research Protection Office website, http://hrpo.wustl.edu. To offer input about your experiences as a research participant or to speak to someone other than the research staff, call the Human Research Protection Office at the number above.

This consent form is not a contract. It is a written explanation of what will happen during the study if you decide to participate. You are not waiving any legal rights by agreeing to participate in this study. As a participant you have rights and responsibilities as described in this document and including:

- To be given enough time before signing below to weigh the risks and potential benefits and decide if you want to participate without any pressure from the research team or others.
- To understand all of the information included in the document, have your questions answered, and receive an explanation of anything you do not understand.
- To follow the procedures described in this document and the instructions of the research team to the best of your ability unless you choose to stop your participation in the research study.
- To give the research team accurate and complete information.
- To tell the research team promptly about any problems you have related to your participation, or if you are unable to continue and wish to stop participating in the research study.

Your signature indicates that this research study has been explained to you, that your questions have been answered, and that you agree to take part in this study. You will receive a signed and dated copy of this form.

Do not sign this form if today's date is after EXPIRATION DATE: 03/10/21.

_____ _____
(Signature of Participant) (Date)

_____
(Participant's name – printed)

Statement of Person Who Obtained Consent

The information in this document has been discussed with the participant or, where appropriate, with the participant's legally authorized representative. The participant has indicated that they understand the risks, benefits, and procedures involved with participation in this research study.

_____ _____
(Signature of Person who Obtained Consent) (Date)

_____
(Name of Person who Obtained Consent - printed)