Washington University in St. Louis

INFORMED CONSENT DOCUMENT

Project Title: ASSESSMENT OF FUNCTIONAL STATUS OF ESTROGEN RECEPTORS IN BREAST CANCER BY POSITRON EMISSION TOMOGRAPHY

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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 any 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 have been diagnosed with new, advanced, metastatic or recurrent breast cancer and your doctor is planning to treat you with endocrine therapy (ET). Your tumor has been tested for series of factors including estrogen receptor (ER), progesterone receptor (PR) and a protein called human epidermal growth factor (HER2). Patients whose tumors are hormone receptor positive (ER+ & / or PR+) can be treated with ET which is less toxic and has less side effects compared to chemotherapy treatments. Based on your test results your doctor has recommended that ET is the best treatment option for you.

One problem with the current way breast cancers are diagnosed and treatment decisions are made is that we must rely on biopsies or small samples of tissue that are taken from the tumor to tell us what types of cancer cells are present. A tumor may not be uniform in the type of cells present so the biopsy sample may not accurately represent the actual function of the cells within the tumor. Additionally, just because a tumor was classified as, for example, ER+ at initial diagnosis recurrent or metastatic tumors may not have the same characteristics.

The purpose of this research study is to see if a radioactive tracer called ([18F]fluoro-16α,17α-[(R)-1'-α-furylmethylidene)dioxy]-19-norpregn-4-ene-3,20 dione) (also referred to as ^{18}F-FFNP) with positron emission tomography (PET) scanning can provide more information about your response to ET. The PET scanner is actually a combination PET scanner and a computed tomography (CT) or computed axial tomography (CAT) scanner. It is often called a PET/CT scan. ^{18}F-FFNP is a radioactive form of the hormone progesterone. ^{18}F-FFNP is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration.

Endocrine therapy works by blocking or lowering the amount of estrogen hormone in your body. ^{18}F-FFNP-PET/CT scanning is a way to determine the amount of working hormone receptors throughout your body.

WHAT WILL HAPPEN DURING THIS STUDY?

^{18}F-FDG PET/CT Imaging: If you have not recently undergo imaging which can be used to determine the site(s) of metabolically active cancer cells in your body you will be asked to undergo a ^{18}F-FDG PET/CT scan. FDG is a radioactive form of sugar and an FDG-PET/CT scan identifies cancer cells in the body based upon the amount of sugar they use. For the FDG PET/CT scan you will be asked not to eat anything for at least 4 hours before the scan. On the day of the scan a small IV will be placed in a vein of your arm. The IV will be used to collect a small sample of blood (less than 1 teaspoon) and will be used to test your blood sugar or glucose level. If your glucose level is within test limits you will receive the FDG medication into your IV line. The FDG will be allowed to circulate in your body for about 60 minutes. During this time you might be asked to drink water or you may be given IV solution (saline) through your IV line to ensure you are well hydrated. After the FDG has circulated you will be asked to empty your bladder in the restroom before being placed on the scanning table for pictures. The scan will take 20-30 minute and your total visit time will be 2 ½ - 3 hours. If you have recently had this test or similar type of scan performed it may not be necessary to repeat the FDG-PET/CT scan for study purposes.

^{18}F-FFNP PET/CT Scanning: For this research project your will be asked to undergo two ^{18}F-FFNP-PET/CT scans before you begin treatment with ET. The first scan will be a baseline scan which will identify the sites of cancer which are hormone positive. The second scan will be performed after a 1-day estradiol challenge test. Both ^{18}F-FFNP-PET/CT scans will be performed in the same way. On the day of the scan there are no restrictions. You may eat and drink like normal and take all your normal medications. A small IV will be placed in a vein of your arm. The IV will be used to collect a small sample of blood as described below and for the injection of the ^{18}F-FFNP study medication. After you receive ^{18}F-FFNP you will be asked to rest comfortably for approximately 30-40 minutes while it circulates in your body.

After the FFNP has circulated you will be asked to empty your bladder in the restroom for the scan. You will be positioned on the imaging table with your arms resting above your head or secured to your side for the scan. It will take about 20-60 minutes to complete your scan. The amount of time depends on several factors including your height and weight, how much ^{18}F-FFNP you received and where your tumor(s) is located in your body. The total amount of you will need to be at the PET facility for the scan is approximately 3 -3 ½ hours.

Vital Sign Assessment: Your vital signs (blood pressure, heart rate, breathing rate and temperature) will be recorded before you receive the injection of 18F-FFNP, within 30 minutes after the injection and after the scan is complete.

Follow up Phone Call: The day after your ^{18}F-FFNP-PET/CT scan you will be contacted by the study coordinator for a quick follow up conversation. The purpose of this is to review with you how you are feeling and to see if you had any problems related to the injection of ^{18}F-FFNP, or the scan. On the day of the 2nd scan you will be questioned to see if you had any problems related to the estrogen medication

given to you as part of the estradiol challenge test.

Blood Samples for Laboratory Testing: A small sample of blood (less than 2 teaspoons) will be taken from your IV line after it has been placed and before you receive your injection of ^{18}F-FFNP on each of the scanning days. This blood sample will be tested at a later date and time using a very sensitive test to measure the amount of estrogen in your blood stream. The results of these tests will be compared with your scan and also with your overall response to treatment.

Estradiol Challenge Test: Within 2 weeks of your baseline scan you will be scheduled to return to the PET facility for your 2nd ^{18}F-FFNP-PET/CT scan. This scan will be scheduled to be close to your estradiol challenge test. For the estradiol challenge test you will be given a total of 6 mg of the medication estrogen. The estradiol medication will be provided to you from the study and given to you by a coordinator or physician working with the study. The 6 mg will be in the form of three 2 mg tablets which you will take orally (by mouth). You will be asked to take one 2 mg tablet three times spaced approximately 8 hours apart. Approximately 8-48 hours after you take your last tablet of estrogen you will be scheduled to return to the PET facility for your 2nd scan. The purpose of the estradiol challenge test is to identify how metabolically active the hormone receptors within the cancer are. We believe a change in the tumor uptake following a 1-day estradiol challenge will be predictive of those women who are going to respond best to ET. The 2 tables below are SAMPLE study calendars of how this could be scheduled:

Tuesday: Baseline FFNP-PET/CT Scan Appointment @ 11:30	Wednesday start estradiol challenge Take one 2mg tablet @ 2pm Take one 2mg tablet @ 10 pm	Thursday: Take one 2mg tablet @ 6AM FFNP-PET/CT scan @ 2PM

OR

Friday: Baseline FFNP-PET/CT Scan	Saturday start estradiol challenge Take one 2mg tablet @ 10 PM	Sunday: Continue estradiol challenge Take one 2 mg tablet @ 6AM Take one 2 mg tablet @ 2 PM	Tuesday: FFNP-PET/CT scan @ 2PM

If you need to have an FDG-PET/CT scan for study purposes it must be done on a day different from FFNP PET/CT scans. It can be done either before or after the first FFNP PET/CT scan but must be done before the estradiol medication is given.

Standard Endocrine Therapy Treatment: After your second ^{18}F-FFNP PET/CT scan you will begin your treatment with endocrine therapy as prescribed by your doctor. Endocrine therapy is standard of care. You are not required to receive any special type of endocrine therapy as part of this research project. What you receive, how you are instructed to take your medication, and how often you follow up with your doctor will be determined by your doctor who treats you for breast cancer. The study will follow your medical records to see how well you respond to treatment. The study will follow your medical records until you are no longer receiving endocrine therapy. The information collected from your chart will include any test results that were ordered to determine your response to therapy: scanning such as CT, or bone scan, magnetic resonance imaging (MRI), ultrasound or mammography, and laboratory or pathology test results. The study will also look at any notes such as history and physical exam, treatment notes, or treatment team correspondence related to your treatment and response to

treatment.

Your FDG PET/CT scan if done for study purposes will be reviewed by a radiologist and the results and images will be made part of your medical record so that the doctor(s) who treatment you may have this additional information. The results of your FFNP-PET/CT scans are not meant to be used to determine or change the treatment you will be receiving. The FFNP-PET/CT scan will be reviewed by the study doctor and discussed with the doctor who referred you to the study. The FFNP-PET/CT scan results will not be part of your medical record and the images will be used for research purposes only.

Will you save my samples or research data to use in future research studies?

As part of this study, we are obtaining PET/CT images from you. We would like to use this PET/CT images 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 breast cancer, 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 images you give up any property rights you may have in the PET/CT images.

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

HOW MANY PEOPLE WILL PARTICIPATE?

Approximately 50 people will take part in this study conducted by investigators at Washington University.

HOW LONG WILL I BE IN THIS STUDY?

If you agree to take part in this study, your active involvement will last for up to 6 days.

- If you receive an FDG-PET/CT scan about 2 ½ - 3 hours of your time will be needed
- Each ^{18}F-FFNP-PET/CT will require about 3 – 3 ½ hours of your time (2 scans)
- Each follow up phone call will require 5 minutes or less of your time (2 phone calls)
- Estradiol challenge – this does not require a visit to the hospital but you will be required to take the estrogen medication as directed over the course of a 24 hour period. Depending on the timing this may require you to wake up earlier than you normally do or to set an alarm clock to take the medication at the times prescribed.

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.

^{18} F-FDG Injection:

Likely/Common: pain or discomfort at the injection site.

- **Rare:** There is a rare possibility of an allergic-type or other adverse reaction to radioactively labeled drugs. While none have been reported to date with the radioactive material FDG, such a reaction could be serious and may result in death.

^{18}F-FFNP- Injection: The amount of progesterone in the radioactive tracer ^{18}F-FFNP is very small and is no side effects from the progesterone itself are expected. The following side effects have been noted when progesterone is given at much greater doses than is used in this study:

Likely/Common

Mild

- pain at the injection site
- upset stomach
- changes in appetite
- generalized feeling of weakness or fatigue
- fever
- headache

Less Likely/Less Common

Serious

- weight gain
- fluid retention
- insomnia (unable to sleep) or drowsiness
- breast discomfort or enlargement

Rare

Life Threatening

- allergic reaction and symptoms such as-unexplained rash, itching, hives, and swelling, irregular heartbeat, difficulty breathing and shortness of breath.

Estradiol Challenge Test: The following side effects have been reported by patients taking estradiol as treatment for breast cancer. The dose of estradiol you will receive for the challenge test is much smaller than the treatment dose.

Likely/Common

Mild

- upset stomach
- nausea

- vomiting
- changes in appetite
- generalized feeling of weakness or fatigue
- fever
- headache

Less Likely/Less Common

Serious

- weight gain
- fluid retention
- insomnia (unable to sleep) or drowsiness
- vaginal discharge
- spotting to darkening of the skin
- breast discomfort or enlargement

Rare

Life Threatening

- uterine fibroids
- stroke
- blood clots
- allergic reaction and symptoms such as-unexplained rash, itching, hives, and swelling, irregular heartbeat, difficulty breathing and shortness of breath.
- There is a rare possibility that the administration of estrace will cause symptoms of clinical flare. Clinical flare can occur with any hormone used in the treatment of breast cancer. Physicians recognize that women who experience a clinical flare are likely to benefit from hormone therapy. Clinical flare is a temporary worsening of the symptoms associated with your breast cancer such as increased bone and joint pain.

While it is rare, clinical flare is most often seen during the first weeks of treatment with estradiol and other forms of hormonal therapy. The small dose of estradiol you are given for only a single day is not expected to cause a noticeable flare reaction. The small dose is meant to cause changes at the cellular level that can be detected on the PET/CT imaging.

PET/CT Imaging:

Mild / Likely: Discomfort from lying still on the imaging table
Rare: Malfunction of worn or implanted electronic medical devices.

If you have electronic medical devices implanted such as a pacemaker or a drug pump, please make sure you tell your study doctors and research staff. The CT scan may cause a malfunction of electronic medical devices.

Radiation Exposure: This study will expose you to radiation from the injection of the PET study medication ^{18}F-FDG and the investigational radioactive drug, ^{18}F-FFNP, and from CT scanning used as part of each PET/CT scan. The amount of radiation from one FDG PET/CT scan when averaged over your entire body, is 30% of the amount a person who works with radiation is allowed to have in one

year. The amount of exposure from is ^{18}F-FFNP-PET/CT scan is equivalent to approxately 28% of the amount a person who works with radiation is allowed to receive in on year. The maximum amount you will receive is from 1 FDG and 2 FFNP-PET/CT scans which is approximately 86% of the allowable annual dose for a radiation worker. 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.

IV Placement and Blood Drawing:

Likely/Common
Mild
- discomfort from placement of the IV in your arm or hand or from the needle used to draw blood

Less Likely/Less Common
Serious
- There is a slight risk of bruising
- Some people feel dizzy or faint when an IV is placed or blood is drawn from them

Rare
Life Threatening
- There is a rare risk of infection at the site of IV placement or blood drawing.

Vital Signs: You may feel discomfort from the squeezing of the blood pressure cuff around your arm.

Participation in future research studies: Treatments in this study may disqualify you for other research studies.

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 being able to accurately determine who will and will not benefit from endocrine therapy as primary treatment for breast cancer can prevent unnecessary treatments and treatment related side effects.

WILL IT COST ME ANYTHING TO BE IN THIS STUDY?

You may have additional costs for being in this research study.

- You will be asked to visit the hospital for two separate visits. If you are making the trip to the hospital only for the research visits you will have travel related expenses.

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 because payment will be made in the form of a check mailed to you. It can take up to 4-6 weeks for processing and delivery of the check to the address you provide. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

You will receive $100 for each ^{18}F-FFNP-PET/CT imaging session. If you also need to have a FDG-PET/CT scan you will receive an additional $100. If you complete both FFNP imaging session on study you will receive a total of $200. If you receive 1 FDG-PET/CT scan and 2 FDG-PET/CT scans you will receive a total of $300. If you do not complete both FFNP PET/CT scans, you will be paid for the scan you complete. If you receive any one of the injection(s) but are not able to complete the scan you will be paid $25. You will also be provided coverage for parking expenses. Overnight hotel stay(s) may be available if needed as well.

WHO IS FUNDING THIS STUDY?

The National Institutes of Health is funding this research study. This means that Washington University is receiving payments from the National Institutes of Health to support the activities that are required to conduct the study. No one on the research team will receive a direct payment or increase in salary from the National Institutes of Health for conducting this 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 Dr. Farrokh Dehdashti at 314-362-1474 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 National Institutes of Health
- Your primary care physician if a medical condition that needs urgent attention is discovered
- Hospital or University representatives, to complete Hospital or University responsibilities
- Information about your participation in this study may be documented in your health care records and be available to your health care providers who are not part of the research team.
- 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.

The Siteman Cancer Center at Washington University School of Medicine and Barnes-Jewish Hospital is supported by funding from the National Cancer Institute (NCI). To meet NCI requirements, your protected health information relating to your participation in this study (including your social security number) will be stored in a secure database at the Siteman Cancer Center. This database and also your health care records may be reviewed by Siteman Cancer Center personnel. All information will be securely and confidentially maintained.

To help protect your confidentiality, we will store all paper documents behind two locks. All electronic data will be password protected and stored on a password protected computer. Your blood samples will be temporarily stored in a locked freezer behind two locks. Blood samples will be processed in groups or batches. Once processed, they will be destroyed as biological waste and not kept for any future testing. 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.

This consent form or similar documentation that you are participating in a research study may be included in your health care record. Anyone with access to your health care record, including your health insurance company may be able to see that you are participating in a research study.

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

To further protect your privacy, this research is covered by a Certificate of Confidentiality from the federal government. This means that the researchers can refuse to disclose information that may identify you in any legal or court proceeding or to anyone who is not connected with the research except if:

- there is a law that requires disclosure, such as to report child abuse and neglect, or harm to self or others*;*
- you give permission to disclose your information, including as described in this consent form; or
- it is used for other scientific research allowed by federal law.

You have the right to share your information or involvement in this study with anyone at any time. You may also give the research team permission to disclose your information to a third party or any other person not connected with the research.

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 send 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 in 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 researchers might decide to end your participation in this research study earlier than planned. This might happen for no reason or because staying in the study would be harmful, you need treatment that is not allowed while on the study, you fail to follow instructions, you develop a major side effect, or the study is canceled.

WHAT IF I HAVE QUESTIONS?

We encourage you to ask questions. If you have any questions about the research study itself, please contact: Dr. Farrokh Dehdashti at 314-362-1474. If you experience a research-related injury, please contact: Dr. Farrokh Dehdashti at 314-362-1474.
If you have questions, concerns, or complaints about your rights as a research participant, please contact the Human Research Protection Office, 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 web site, 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: 02/18/20.

_____ _____
(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)