Fred Hutchinson Cancer Research Center
University of Washington

CONSENT TO TAKE PART IN:

Study Title: Serial [F-18] fluoroestradiol (FES) PET Imaging to Evaluate Endocrine-Targeted Therapy

Principal Investigator

Hannah Linden, M.D.
University of Washington
Seattle Cancer Care Alliance
825 Eastlake Avenue East
Seattle, WA 98109-1023
(206) 606-6355

Emergency number (24 hours): (206) 598-6190 (paging) for Dr. Linden or the Nuclear Medicine Resident on call

Important things to know about this study.

You are invited to participate in a research study. The purpose of this research is to look at a new type of imaging (Serial [F-18] Flouroestradiol (also called F-18 FES) PET) to see if it may give doctors helpful information about a particular patient's cancer.

People who agree to join the study will be asked to attend about 3 visits over a year. The study involves having two types of scans, having a small amount of blood drawn, and receiving a biopsy (or allowing us to use tissue from a recent biopsy you received as part of your medical care). The two types of scan you will receive use two different tracer compounds: F18-FES and F18-FDG. F18-FES is an *Investigational Product*, meaning that it is a product that is not yet approved by the FDA for this use, and F18-FDG is a *standard of care* product, meaning that it is approved for this use and could be used in your normal medical care.

We do not know if F-18 FES would help treat breast cancer, and it could even make your condition/disease worse. F-18 FES could cause side effects such as bruising at the injection site or minor changes in taste and smell, as described in this form.

You do not have to join this study. You can choose to receive standard methods to treat breast cancer instead of participating in this study. We will give you details about the purposes, procedures, risks and possible benefits related to this study. We will explain other choices that you have. We will also give you any other information that you need in order to make an informed decision about joining this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

Why is this study being done?

The purpose of this study is to measure the amount of estrogen receptor in your breast cancer using an imaging procedure called Positron Emission Tomography (PET). Estrogen receptors are substances found in normal breast tissue and some breast cancers that cause the cancers to grow when the female hormone, estrogen, is present. [^{18}F]-fluoroestradiol (FES) is a specialized radioactive PET tracer used to detect whether or not tumors contain estrogen receptors. Estrogen receptors are proteins that make tumors sensitive to hormones, such as estrogen. Breast tumors with estrogen receptors can behave differently than those without estrogen receptors and will often respond to different forms of treatment. In this study, we will use FES to form images of estrogen receptors in tumors in the breast or other sites in the body. FES is an investigational or experimental imaging agent that has not yet been approved by the Food and Drug Administration for use in this cancer imaging.

[^{18}F] -Fluorodeoxyglucose (FDG) is a PET tracer that allows us to see how tumors use glucose, a sugar. This FDG PET scan is normally done in breast cancer patients as part of normal clinical care to measure the spread of breast cancer. In this study the baseline FDG PET scan will likely be part of your standard medical care but additional follow up FDG PET scans (up to 2) that are done for the study will be considered research scans.

In this study, we want to find out how accurate and useful FES is in imaging breast cancer patients and how our imaging measures change with therapy. The therapy is not a part of this trial. You will receive the therapy in a setting of either standard care or another trial. The results of the PET scans will be compared with other information that is obtained as part of your normal care about how you respond to hormonal treatment and changes in the measures after you have had treatment.

In addition, some patients on this study may agree to provide a tissue sample from a site of their disease. An analysis of levels of estrogen receptors and intra-tumor steroid hormones will be performed on these samples in a laboratory. This will allow us to compare the results of scans with results of microscopic tissue evaluation and gain even better understanding of ways in which tumors respond to treatment.

How many people will take part in the study?

Up to 20 people will take part in this study. All patients will have an FES PET scan before beginning new treatment with hormonal targeted therapy and return for follow up FES and FDG PET scans up to 2 additional times during the course of treatment.

What will happen if I take part in this research study?

Your participation in this study is voluntary. You may refuse to take part in the study with no penalty of loss of benefit to you. You may stop participation in this trial at any time without any penalty or loss of benefits to which you would otherwise be entitled.

People who participate in this study must have breast cancer and must be willing to undergo the FES PET and FDG PET scans and return for follow up FES and FDG PET scans up to two times during the course of treatment (depending on what medication you are receiving).

Participation in this trial will continue actively for at least one (1) year after the first scans. We will also have access to medical information related to your cancer treatment for up to 20 years. During this time, we may also contact you to see how you are doing.

If you agree to participate in this research, you will have an FES PET scan that will be performed at the University of Washington Medical Center. This scan will be performed before you start new treatment for your breast cancer. Depending on what type of treatment you are getting we will have you return for up to two (2) additional FES and FDG PET scans over the course of up to 6 months. In Nuclear Medicine scans, imaging is done with specialized cameras that can pick up the tiny radiation signals given off by the tracer and determine where the signals come from. In this way, we can form a picture of where the tracers go after they are injected. The type of scan we will perform is called a Positron Emission Tomography (PET) scan, which uses a large doughnut shaped detection device to provide a map of where tracers go.

Each PET scan will require a total of about one half day of your time. The scan will take place using our PET scanner, which is located in the Nuclear Medicine clinic. You will lie on a comfortable table for up to 1 hour, while your head or body sits in the opening of the PET device. About half of this time is used for actual imaging while the other half is needed for various preparations.

We will inject [^{18}F] -Fluoroestradiol (FES) into your vein. Approximately 4 teaspoons of blood will be withdrawn and sent to the laboratory to measure the amount of natural hormones and proteins in your blood. The PET machine will collect information for about 45 minutes starting 1 hour after the injection of the FES. You will not be charged for this scan.

FDG PET scans will be done at the same location as the FES scans or at the Seattle Cancer Care Alliance. Those will also take about a half-day of your time. We would need to do the FDG scan within a week or two of the FES scan, but on different days. Most of the time the FDG scan will be done before the FES scan. We will inject FDG into your vein. The PET machine will collect information for about 45 minutes starting 1 hour after the injection of the FDG. Information from this FDG scan will be compared to information gathered from the estrogen imaging scan (FES scan).

The scans done for this study will be compared with the information contained in your medical record. This will include the results of FDG PET scans, physical examination, laboratory studies, CT scans, MRI scans, bone scans, and other imaging scans that are done as part of standard care.

Catheter placement: For each scan, small tubes will be inserted into one or two veins, most likely one in each arm. One tube will be used to inject the tracer while the other tube, if necessary, will be used withdraw small blood samples that will be tested for the amounts of each tracer. A central line or a chest port may be used for the blood draws in place of the second tube in the vein. The tubes in your veins will be removed at the end of the scans.

Optional biopsies: We would like to measure the changes in hormone expression in your tumor. If you have a site of cancer that is easily accessible, we would like to obtain a biopsy before you start your new treatment and, potentially, repeat the biopsy once, after you have been on the therapy for at least 1 week, to up to 12 weeks. If you are having a biopsy performed as standard of care during one or both of those time points, we can obtain a sample for research during that procedure, eliminating a need for a separate research biopsy. If we are not able to obtain a biopsy or you prefer not to have one before you start treatment, we can obtain part of your tumor that was biopsied and archived earlier in the course of your disease. However, some research tests do not work on archival samples. In any case, we will ask your permission upfront and you can agree or decline. Your decision will be marked in the optional biopsies section at the end of this consent form.

In addition, 3 teaspoons of blood may be withdrawn at the time of biopsy to allow comparison of steroid hormone levels in biopsied tissue and blood.

Study Chart

The procedures listed in the previous section are outlined in the table below:

Time Point	What You Do
Day of FES PET 1 scan	• Check in at the Seattle Cancer Care Alliance Clinic or University of Washington Nuclear Medicine Clinic for an FES PET scan • Have IVs placed and blood drawn to test hormone levels
Before therapy start	• Optional tumor biopsy #1 and blood draw (if you agree to this at the end of this consent form)

Weeks 1-12	• Begin new treatment
	• FES PET 2 scan and FDG PET 2 scan on separate days; FDG PET 2 may be omitted on certain therapies
	  • Before each FES scan:
	  • Intravenous Catheter Placement
	  • Blood draw (4 teaspoons)
	  • Before each FDG scan:
	  • Intravenous Catheter Placement
	• Standard clinical imaging if ordered by your doctor (may include bone scan,

	CAT scan, ultrasound, X-rays, MRI scan) • Blood tests drawn on the day of FES PET scan • Optional repeat tumor biopsy #2 and blood draw (if you agree to this at the end of this consent form)
Weeks 13-24 after FES PET 2 (applicable only on certain therapies)	• Continue treatment • FES PET 3 scan andFDG PET 3 scan on separate days • Standard clinical imaging if ordered by your doctor (may include bone scan, CAT scan, ultrasound, X-rays, MRI scan) • Blood tests drawn on the day of FES PET scan • There is no biopsy with blood draw planned at this time point
Clinical follow up	• Continue treatment for your breast cancer • We will access your health record to see how you're doing. If your health record does not contain information on your current status, we may contact you.

Before you begin the study …

You may need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Standard Imaging (Bone scan, CAT Scan, ultrasound, chest x-ray or MRI scan as ordered by your doctor)
- FDG PET Scan (clinical scan at before starting treatment)
- Physical Exam
- Blood samples: (requiring less that an ounce, i.e. 2 teaspoons, of blood) will be taken from a vein in your arm or from your port. The following tests will be done:
  - Complete Blood Count, Chemistry panel, Tumor markers (CA27.29 or CEA)
  - A pregnancy test if you are a women who is able to have children. (If you are pregnant or breast feeding you cannot participate in this study)

When I am finished with the baseline PET Scans...

You will begin your new therapy and continue to be followed by your treating doctor to measure how you respond to your new medications. You will be asked to return for a follow up FDG and FES PET scan up to 2 times during your treatment. The timing for these scans will be determined by what type of treatment you are getting and we will go over the planned schedule for these scans with you before you enroll in the study. Your doctor will order any follow up scans (Bone scan, CAT scan, MRI scans) and blood

draws when they feel it is best. However, if you have not had any scans repeated by three months after the FES PET scan your doctor will be asked to order these so that we can measure your response to the new medication.

How long will I be in the study?

The study doctor will ask you to visit your doctor's office for follow-up exams for up to one year after you enter the study. During this time blood tests and scans will be ordered by your doctor to measure how you are responding to your new medication.

If you withdraw from the study for any reason, previously collected information would remain in the study records and would be included in the analysis of results. This information could not be removed from the study records.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop your participation.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects.

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

Risks and side effects related to F-18 FES PET:

Likely (Most patients are expected to experience)

- Discomfort, bleeding or bruising at the injection site.

Rare (Less than 1% of patients)

- Changes in taste or smell

Potential but Serious (Have never occurred)

The following risks have not been observed in patients receiving FES PET scans. However, scientists have identified reactions that could possibly occur based on what we know about compounds like FES. If you notice any of these, you should contact the study doctor right away.

- Local tissue injury and possible infection due to accidental extravasation of the dose.

- Allergic reaction which may be life threatening
- Transient nausea, vomiting and anorexia
- Abnormal uterine bleeding
- Injury or increased long term risk of a new cancer due to radiation exposure

Risks Related to FDG PET
Fludeoxyglucose (FDG) is an imaging tracer (a compound used to highlight certain proteins or tissues in your body during a scan). It is standard-of-care, meaning that it is a product you could receive if you were not in a research study.

Likely (Most patients are expected to experience)
- Discomfort, bleeding or bruising at the injection site.

Rare (Less than 1% of patients)
- Pruritus
- Edema
- Rash

Radiation Risks (Both FDG and FES)
Some of the tests that you will have in this research study will expose you to radiation. Everyone receives a small amount of radiation every day called "background radiation". This radiation is natural and comes from space, air, water, soil, and the food you eat. Each year you are exposed to about 3 milliSieverts (mSv) of this background radiation. A milliSievert is a unit of radiation dose. There is minimal risk to your health from the amount of radiation you will receive in this study. The usual lifetime risk of getting cancer is 42%. For every 10 mSv you receive, your risk may increase 0.1%. If you have more procedures that expose you to radiation, your risk will go up. For comparison, the estimated radiation dose from each of these tests is listed below:

F-18 FES scan: 5-12 mSv
F-18 FDG scan: 6-19 mSv.

You will not be able to participate in this study if you are pregnant or breast-feeding due to risks to the fetus or child from radiation exposure.

Reproductive risks
Chemotherapy and radiation treatments could cause sterility (unable to have children). The scans in this protocol may involve unknown risks to an embryo, fetus (unborn baby) or nursing infant. Therefore, you could not join this study if you are pregnant, if you are planning to become pregnant, or if you are breast-feeding.

Risks Associated with Biopsies:
Biopsies are normally performed under the guidance of an imaging technique. Each procedure requires a separate consent prior to the biopsy. The risks may include:
- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.

- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other potentially serious complications from bleeding or organ damage may occur. These might require additional surgical intervention.

Blood Draw Risks
The blood draw may briefly cause you to feel faint, lightheaded, nauseated, mild pain, bleeding, bruising and infection at the site of the needle insertion.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other participants with breast cancer in the future.

Other Information

While doctors hope FES PET scans will be more useful measuring changes in tumors or response to certain medications there is no proof of this yet. The results of the FES PET scans and research FDG PET scans will be provided to your treating doctors but will not be used to make decisions about treatment. It is possible that the FES PET scan will find information about your medical condition that need your and your doctor's attention, such as a new tumor site. This information will be provided to you and your physician in a research reports and will be filed in your permanent medical record. The FES PET is experimental and should not be used to decide what to treatment is best for you. By comparing your information to that of patients with the same kinds of cancer who are undergoing similar treatment we are hoping to learn more about how breast cancer grows and develops and identify better ways to follow changes in cancer response to certain treatments. This may help us develop better treatments and imaging tests to treat breast cancer in the future.

What other choices do I have if I do not take part in this study?

You do not have to join this study. You are free to say "yes" or "no". Your regular medical care would not change if you decide to say "no". You have other choices for treatment. Each of these choices has risks and benefits.

Your other choices may include:
- Getting treatment or care for your cancer without being in a study
- Taking part in another study

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

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records pertaining to this study for research, quality assurance, and data analysis include:

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect the rights and welfare of research participants.
- Fred Hutchinson Cancer Research Center, University of Washington, and Seattle Cancer Care Alliance.
- US National Institutes of Health, National Cancer Institute, Office for Human Research Protections, Food and Drug Administration, and other regulatory agencies as required.

Study records will be maintained for up to twenty years following completion of the study.

In order to evaluate the results of this study, all doctors and Researchers linked with the study will need to see your medical records, now and in the future.

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal identity will not be revealed in any reports about the study or results. All precautions will be taken and efforts will be made to keep your medical records and personal information private and confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

How will my specimens and data be used in the future?

In addition, be aware that by agreeing to participate in this study, your information or tissue samples could be used for future research studies or sent to other investigators for future research studies without additional consent from you. These future research studies will be reviewed by an oversight group known as an institutional review board if required by law. The information that identifies you will first be removed from your information

or tissue samples. If you do not want your information or tissue samples to be used for future research studies without your consent, you should not participate in this study.

Medical Record Information

If you receive any services, tests, or procedures at University of Washington clinical facilities ("UW Medicine") or at the Seattle Cancer Care Alliance ("SCCA") as part of this study, information about this study will become part of your medical record. If you do not already have a UW Medicine or SCCA medical record for clinical purposes, one will be created for you. Basic information such as the name and number of the study, the study sponsor, the names and contact information of the study staff will be included in your medical record.

Research procedures and test results may also be put in your medical record. This will include: A research report for each of your research PET scans.

If you have already given or in the future decide to give permission to any person or group (such as an insurance company or employer) to have access to your medical record, the information about this study and your participation in it will be included. This could affect your ability to get life insurance or a new job.

It is important for you to consider the possible risks of including study information in your medical record before you sign this consent form.

This research is covered by a Certificate of Confidentiality from the U.S. government. This Certificate helps protect the confidentiality of information about people who join this study. If you join the study, the Certificate means that generally we would not have to give out identifying information about you even if we were asked to by a court of law. We would use the Certificate to resist any demands for identifying information.

We could not use the Certificate to withhold research information if you give written consent to give it to an insurer, employer, or other person.

This protection has some limits. We would voluntarily provide the information:

- To a member of the federal government who needs it in order to audit or evaluate the research.
- To the funding agency and groups involved in the research, if they need the information to make sure the research is being done correctly.
- To the federal Food and Drug Administration (FDA), if required by the FDA.
- To someone who is accused of a crime, if he or she believes that our research records could be used for defense.
- To authorities, if we learn of child abuse, elder abuse, or if participants might harm themselves or others.

What are the costs of taking part in this study?

You will not be required to pay for the FES-PET, FDG-PET, biopsy, or blood draws. The only expected cost of participating in this study is the cost of transportation and parking at the clinic. You are responsible for these transportation and parking costs.

However, you or your insurer will pay for the costs, if you are having a biopsy performed as standard of care (if your doctor has ordered it for your clinical care, separate from this study). If you are receiving a standard of care biopsy within 30 days of screening or, and if you consented to the optional biopsies, we may use tissue from that biopsy instead of doing a new biopsy. In this case, you or your insurer will pay for the costs of this biopsy.

If you have any questions concerning your financial responsibilities then contact your financial advisor at the SCCA (206-288-1113).

You will not be paid for taking part in this study. Your tissue samples might help researchers develop new products. This research could be done by for-profit companies. There is no plan to share with you any revenue generated from products developed using your tissue samples.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this study?

The UW does not normally provide any other form of compensation for injury. However, the law may allow you to seek payment for injury-related expenses if they are caused by malpractice or the fault of the researchers. You do not waive any right to seek payment by signing this consent form.

You or your insurer will be billed for treatment of problems or complications that result from your condition or from standard clinical care.

It is important that you tell your study doctor, Hannah Linden, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at 206-288-7000.

For a life threatening problem, call 911 right away or seek help immediately. Contact your study doctor when the medical emergency is over or as soon as you can.

What are my rights if I take part in this study?

You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.

If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.

During the study, we may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you change your mind about being in this study. If we learn these kinds of information, we will tell you

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Clinicaltrials.gov Posting

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.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor, Hannah Linden at (206) 606-6355.

If you have any questions about your rights as a research participant, please contact 206-667-5900 or email irodirector@fredhutch.org (Director of Institutional Review Office, Fred Hutchinson Cancer Research Center). You may also contact the Human Subjects Division at the University of Washington at (206) 543-0098.

We would like you to allow us to do additional tests on your blood or biopsy specimens:

We would like to measure the changes in estrogen receptor expression and hormonal levels in your tumor. Therefore we would like to obtain a tumor biopsy before you start your new treatment and, potentially, repeat the biopsy once, after you have been on the therapy for at least 1 week, to up to 12 weeks. If you are having a biopsy performed as standard of care during one or both of those time points, we can obtain a sample for research during that procedure, eliminating a need for a separate research biopsy. If we are not able to obtain a biopsy or you prefer not to have one before you start treatment, we can obtain part of your tumor that was biopsied and archived earlier in the course of your disease and perform study related tests on such specimen. However, some research tests may not work on archival samples.

In any case, we ask your permission and you can agree or decline. You do not have to agree to these additional biopsies in order to participate in this study. Also, your regular medical care will not change based on this decision.

Please, answer all questions below by circling "Yes" or "No":

Do you agree to undergo a baseline optional biopsy for this study before you start new treatment? (circle one)

YES **NO** Initials: Date:

Do you agree to undergo one optional repeat biopsy after 1-12 weeks on the treatment? (circle one)

YES **NO** Initials: Date:

If you are having a tumor biopsy performed as standard of care, do you give us permission to obtain a tissue for this study during this procedure? (circle one)

YES **NO** Initials: Date:

If we are not able to obtain a biopsy or if you prefer not to have one before you start treatment, do you give us permission to obtain part of your tumor that was biopsied earlier in the course of your disease, before enrollment on this study? (circle one)

YES **NO** Initials: Date:

We will take a sample of your blood at the time of your FES PET scans and we would like to have your permission to store a small amount of your blood for additional tests related to hormone levels in your blood (examples of the type of tests that may be done are: Estradiol, Estrone, Testosterone, Sex Steroid Binding Proteins or other tests related to hormones in your blood). The results of these tests will not be recorded in your medical record. Those will be used only for the purposes of this study and will not impact your clinical care. You will not be charged for any of the additional tests.

In addition, if you consented to optional biopsies, you may be asked to donate another blood sample at the time of the biopsy, to allow comparison of steroid hormone levels in blood and tissue. These results will not be recorded in your medical record and will not impact your clinical care. You will not be charged for these tests.

Is it OK for us to draw a small amount of your blood at the time of FES PET scans and store it for additional study related tests?

(circle one)

YES **NO** Initials: Date:

Is it OK for us to draw a small amount of your blood for study related tests at the time of optional biopsy?

(circle one)

YES **NO** Initials: Date:

Signatures

Please sign below if you:

- **have read this form (or had it read to you);**
- **had the opportunity to ask any questions you have;**
- **had the opportunity to discuss the research with the person obtaining consent; and**
- **agree to participate in this study.**

Participant:

Printed Name	**Signature**	**Date**

If you served as an interpreter or impartial witness during the consent process, sign below to indicate you attest to the accuracy of the presentation and the participant's apparent understanding of and willingness to participate in the research.

Impartial Witness or Interpreter:

Printed Name	**Signature**	**Date**

Researcher's statement

I have discussed the research study, including procedures and risks, with the person signing above. A copy of the signed consent form will be given to the participant.

Person obtaining consent signature:

Printed Name	**Signature**	**Date**

Protocol: RG1007834
Current consent version date: 11-27-2019
Previous consent version date: n/a
Copies to: EMR

FHCRC IRB Approval
11/17/2020
Document Released Date