EXPLORER PET/CT: Evaluation of Healthy Individuals fromRacial/Ethnic Minority Populations

NCT04812080

Protocol 1714742 including statistical analysis plan

And

Consent

09/14/2021

1) Protocol Title

Title: *EXPLORER PET/CT: Evaluation of Healthy Individuals from Racial/Ethnic Minority Populations*

Principal Investigators: Moon S. Chen, Jr., Ph.D., M.P.H., Professor; Lorenzo Nardo, M.D., Ph.D., Associate Professor
Protocol Version Date: *09/14/2021*

2) Objectives

- Using the total-body PET/CT scanner, gather preliminary data from racial/ethnic minority healthy volunteers to compare with patients with tumors
- Conduct quantitative, genetics-based estimates of ancestry (e.g., African, Chinese, Colombian, Western European, Mexican, Vietnamese, etc.) in racial/ethnic minority healthy volunteers
- Compare participants' self-reported racial/ethnic identity with the quantitative, genetic-based estimates of ancestry

3) Background

The EXPLORER PET/CT scanner is the world's first and only FDA-cleared Total-Body scanner and the world's first device to offer the ability to tomographically image all body parts simultaneously. It has a signal sensitivity gain of ~40 fold compared to existing commercial devices for total-body applications. Spatial resolution is also comparable to or better than all other commercial clinical devices available today. The EXPLORER scanner allows for (a) substantial reduction in scan times or (b) substantial improvements in image quality or (c) substantial reduction in administered activity or (d) combination of (a-c) and (e) total-body coverage. [1-3] With its unprecedented and unmatched potential for cancer detection and characterization, exploiting EXPLORER may result in detection of tumors while they are at earlier stages, and improving the management of cancer therapy throughout the course of the disease.

One specific gap with ongoing research out of the EXPLORER Molecular Imaging Center (EMIC) is the need to have "healthy" (non-cancer) participants.
The aim of this pilot study is to increase the number of healthy individuals from racial/ethnic minority populations. This will advance research being conducted at EMIC by providing "controls" or comparisons to differentiate between images from patients with cancer versus healthy people of the same racial/ethnic ancestry. In addition, blood samples from participants to this study will be utilized for quantitative, genetics-based estimates of ancestry (e.g., African, Chinese, Colombian, Western European, Mexican, Vietnamese, etc.), which is especially valuable in the case of admixed individuals. In order to accomplish this, we will utilize the UCDCCC's Genomics Shared Resource (GSR) for Whole-exome sequencing (WES) and contemporary computational analyses.

1. Cherry SR, Badawi RD, Karp JS, Moses WW, Price P, Jones T. Total-body imaging: Transforming the role of positron emission tomography. Science Translational Med 2017; 9: eaaf6169
2. Cherry SR, Jones T, Karp JS, Qi J, Moses WW, Badawi RD. State of the Art Review.

Total-body PET: maximizing sensitivity to create new opportunities for clinical research and patient care. J Nucl Med 2018; 59: 3-12.

3. Badawi RD, Shi H, Hu P, Chen S, Xu Y, Price PM, Ding Y, Spencer BA, Nardo L, Liu W, Bao J, Jones T, Li H, Cherry SR. First human imaging studies with the EXPLORER total-body PET scanner. J Nucl Med 2019; 60: 299-303

4) Inclusion and Exclusion Criteria

Inclusion criteria:

- Men and women, 18 years of age or older
- Member of a Federally recognized racial/ethnic minority population, e.g., African American or Black; Hispanic or Latino; Asian American; Native Hawaiian or Other Pacific Islander; Native American or Alaska Native
- Willing and able to fast for at least 6 hours before and for the duration of the scan
- Willing to provide blood samples for ancestry analysis
- Willing and able to lay motionless in a supine position for up to 60 minutes and for up to 20 minutes at two separate timepoints
- Willing and able to give informed consent, personal contact information (phone number, email and postal address), insurance information, and primary care physician contact

Exclusion criteria:

- No Primary Care Physician
- No health insurance
- Body weight more than 240 kg (529 pounds)
- Any known concomitant acute infection (including upper respiratory infection, genitourinary infections, etc.)
- History of metastatic or newly (last 5 years) diagnosed locally invasive cancer
- Chemotherapy in the last 5 years
- Radiation therapy in the last 3 years
- Major surgery within the last 6 months
- Pregnancy or breast-feeding
- Diabetes
- Fasting blood glucose level > 200 mg/dL before administration of fluorodeoxyglucose (FDG)
- Prisoners
- Self-reported history of dysphoria or anxiety in closed spaces

5) Study Timelines

- Subject participation: Each subject will participate for up to approximately 3 hours
- Enrollment duration: We anticipate completing enrollment within 18 months.
- Primary data analysis duration: We anticipate completing primary data analysis within 24 months.

6) Study Endpoints

A. To collect preliminary data about total body FDG perfusion and early biodistribution in a cohort of racial/ethnic minority volunteers
B. To allow the study team to supplement participants' self-reported racial/ethnic identity and ancestral origin with Ancestry Informative Markers (AIMS) analysis.

7) Procedures Involved

Subject recruitment

Up to 20 subjects will be recruited for this study. Outreach to both ethnic media and mainstream media outlets will be incorporated into the communications plan for the study, with news releases tailored to Asian, African American and Latino print, radio and TV. To increase the chances of achieving earned media and to build trust with diverse audiences, newsrooms will be supplied with video (b-roll) and interviews (soundbites) conducted with racially-diverse community advisory board members who took a "ride" on the EXPLORER during a tour of the facility and were interviewed about their experience afterwards.

We will also include a paid Facebook campaign that will drive qualified leads to the EXPLORER's StudyPages. The targeted audience will be Sacramento-area residents ages 18 and older with an emphasis on racial/ethnic minorities (African Americans, Asian Americans, and Latinos). Lastly, we will use a recruitment flyer to share with potential candidates and community members.

Study procedures

Consenting and screening: Informed consent for this study will be obtained through a method approved by UC Davis. Consenting and screening for this study will occur not earlier than 4 weeks before the imaging visit. During screening, subjects will be asked to self-disclose their racial/ethnic population affiliation.

Imaging Visit: Participants will be asked to fast for 6 hours prior to arriving at EMIC on the day of their PET imaging study visit. A technologist will screen the participants to evaluate their readiness for PET scanning using the standard UC Davis Radiology approved form. A urine pregnancy test will be administered at no charge to all participants who are able to get pregnant between 18 to 60 years old, unless documented hysterectomy or bilateral ovarian removal is available. Blood glucose level will be tested using the standard fingerstick method per Radiology's standard operating procedures, at no charge.
Following this, an intravenous (IV) line will be placed by the study PET/CT technologist or study physician and the participant will be positioned supine on the scanner table.
We will also ask all subjects if they had a bowel movementfrom the time they are injected with FDG until they complete their scan(s).
Study participants will be injected with 10 +/- 2 mCi of ^{18}F-FDG using the placed IV line and a 60 minute dynamic scan will begin on EXPLORER. Prior to the dynamic scan, an ultra-low-dose CT scan (less than 1 minute) will be acquired for attenuation correction purposes only. After the dynamic scan, participants will be able to get off the scanner and rest in a quiet room at EMIC.

Ninety (90) minutes after being injected with FDG, participants will be positioned supine

on the scanner table once more. At this time, another ultra-low dose CT scan (less than 1 minute) will be acquired for attenuation correction purposes only. This will be followed by a 20 minute static scan on EXPLORER. After this static scan, participants will be able to get off the scanner bed once more and rest for a few minutes. One-hundred and twenty (120) minutes after being injected with FDG, participants will be positioned supine on the scanner table for the last time. At this time, a low dose CT scan (less than 1 minute) will be acquired once again for attenuation correction purposes. This will be followed by one last 20 minute static scan on EXPLORER. After the scans, the patient will get off the scanner. The IV line will be removed after completion of the study.

AIMS: Prior to the scans, whole blood samples (3-5 mL) will be drawn using a butterfly method with the time recorded. The blood samples will be collected into purple-top tubes and subsequently submitted to the UCDCCC GSRfor isolation of genomic DNA (gDNA) using the Gentra Puregene Blood Kit (Qiagen), which yields genomic DNA of required quality (e.g., purity, high molecular weight) and quantity (>35ug). Whole-exome sequencing will be performed at the UC Sequencing Consortium. Raw sequencing data (FASTQ) will be returned to the UCDCCC GSR for data analysis. Results will be used to estimate the proportion of ancestry from a particular geographical area and to supplement participant's self-reported racial/ethnic and ancestral origin.

The PET/CT images created for this study are for research and are not meant to evaluate the subject's health, as they would be if they were part of a clinical (non-research) visit to the doctor or hospital. The images will not receive any routine clinical review by radiologists who interpret PET/CT scans. This means that some findings may be overlooked or misinterpreted. However, if the PET/CT technologists do notice findings that cause concern, they will notify the Study Radiologist. Additionally, if a member of the research team notices any findings that cause concern while conducting image review for study purposes, they will notify the Study Radiologist. The Study Radiologist will conduct a brief review of part of the study images for quality purposes. If the Study Radiologist thinks a clinical problem is present, one of the IRB-approved study physicians will discuss these possible problems with the subject within 8 weeks or immediately upon recognition of any critical finding that requires immediate and/or urgent intervention as described in the Department of Radiology Critical Findings policy (full dataset of images are sometimes not available for review in less than 3 days). Upon written request, we will provide the subject with a copy of a subset of their CT images to take to the physician of their choosing. A subset of PET images may also be shared with the subject unless the images from the study are clinically uninterpretable. In addition, the sponsor may restrict sharing of PET images due to the nature of the research protocol or to protect intellectual property (e.g. proprietary radiotracers). We will send a standard letter to the designated licensed medical provider identified by the subject along with a copy of the subject's radiology report. The standard letter will state that (i) the subject's images were acquired exclusively for a research study and incidental findings that may be related to a medical condition were observed by a UC Davis radiologist; (ii) the images did not receive any dedicated routine clinical review and findings may have been overlooked or misinterpreted; (iii) the subject's physician can contact the study doctor at any time if there are any concerns regarding the study or the subject's findings. In addition, Dr. Lorenzo Nardo or a designee may contact the research subjects and ask what type of medical follow-up, if any, they received.

If there are findings on any of the scans that can deem the subject as not meeting the inclusion/exclusion criteria (e.g. metastatic disease, marked claustrophobia leading to incomplete scans), this event will be reported and the subject will be excluded from the study. An additional participant will be added to meet the recruitment goal.

Data analysis plan
Image reconstruction and analysis: Data from EXPLORER will be acquired and image quality, quantitative comparisons and preliminary biodistribution data collection will be performed by means of regions of interest (ROIs) drawn in different organs and tissue types where pixel intensity and coefficient of variation within ROIs will be computed and recorded.

Statistical considerations: Since this is a pilot exploratory study on a first-of-its kind scanner, no formal power analysis is presented. Exploratory data analysis will be conducted to examine the distribution of the data. Graphical methods including box-plots and histograms will be employed to examine the distributions of the measures. For all continuous variables, descriptive statistics, including means, ranges, and standard deviations will be computed. Ninety-five percent confidence intervals will be computed for means and proportions to obtain interval estimates of all measurements across image. For categorical data, frequency, proportions, and percentages will be calculated.

Compensation
Participants will be compensated with gift cards at a rate of $25 (upon enrollment and radiotracer injection), plus an additional $25 for each hour of participation: up to 3 hours; maximum total of $100.
There is no compensation associated with initial consenting and screening visit.

8) Data and/or Specimen Management and Confidentiality

☒ I understand that if this study involves the use of the UC Davis Health Electronic Health Record (EMR/EPIC) it also contains the clinical data for Marshall Medical Center (MMC). I understand that MMC patient data cannot be accessed for research purposes and that I must take the necessary steps to ensure that MMC data is not accessed, used, or disclosed for UC Davis Health research purposes.

At the time of acquisition, identifiable information will be entered in the UC Davis system database. Electronic image files, radiation dose reports and pertinent medical information will be stored on the EXPLORER Research Cluster located at EMIC on dedicated encrypted password-protected hard disks and workstations at UC Davis, which project staff may access; in addition, electronic image files, radiation dose reports and pertinent medical information will be stored on the UC Davis radiology department PACS system, Radimetrics dose reporting system and Electronic Medical Record. These files will contain the patient identifiers. When this data is transferred for analysis to any other computer/device which is not encrypted and password protected, it will be anonymized. We will assign participants a unique subject/code number that will be used to identify them in our database. Our data will be in the form of anonymized images and coded medical records recorded in an Excel spreadsheet and images in electronic format. The Excel spreadsheet and the images containing the subjects coded medical records will

be stored in an encrypted password-protected device. We will keep the code key containing subject names/medical record numbers and corresponding subject code numbers in a secured location separate from the data. Only study team will have access tothe data. Requests to use the data will be reviewed by the PI. If approved, PI will provide only de-identified data. Quality control will include regular data verification and protocolcompliance checks by the PI and the study coordinator. The PI will complete annual reports to the UC Davis IRB detailing the study progress and enrollment status.

9) Data and/or Specimen Banking

All the imaging data will be banked indefinitely for future use. Data will be saved on the EXPLORER Research Cluster located at EMIC and/or on dedicated encrypted password-protected hard disks and workstatations at UC Davis with access limited to authorized personnel. In addition, electronic image files, radiation dose reports and pertinent medical information will be stored on the UC Davis Radiology Department PACS system and Electronic Medical Record. A radiation dose report will be generated. This will be part of the banked data and will contain Protected Health Information. It will be sent to Radimetric system, which is a mandated tracking system for lifetime radiation dose.

Future use of bank data may include improved image analysis, use as a normal atlas/comparator, and use for other research purposes.

In addition, investigators from other entities may contact the study team with requests to use banked data. Anonymous data may be shared with other entities if appropriate data use agreements are in place (e.g., DTA, UC Reliance) and if approved by the investigators in charge of this study.

Urine samples and blood samples are used for screening purposes and for AIMS analysis. After the results are recorded these biological specimens will be discarded.

10) Provisions to Monitor the Data to Ensure the Safety of Subjects

Throughout the conduct of this study, study personnel will consult with the UC Davis Health Radiation Safety Officer and the local IRB regarding the monitoring and reporting of adverse events and follow their recommendations. Protocol changes involving the radiation dose will first receive approvals from the Radiation Use Committee prior to submitting a modification request to the IRB.

Participants will be informed about the study risks during the initial consenting and screening visit.

Protocol changes will not be implemented prior to UC Davis IRB approval unless necessaryto eliminate apparent immediate hazards to the research subjects.

If any incidental findings are detected, they will be managed as described above in this protocol.

<u>Data safety monitoring</u>

After acquisition of data, we will assign participants a unique subject/code number that we

will use to identify them in the database used for processing, analysis, or publications. Our coded data will be in the form of elements of medical records recorded in an Excel spreadsheet saved in a encrypted password-protected device. Electronic image files, which may contain PHI, will be stored on the EXPLORER research cluster at EMIC and/or on dedicated encrypted password-protected hard disks and workstations at UC Davis. In addition, electronic image files, radiation dose reports and pertinent medical information will be stored on the UC Davis Radiology Department PACS system, the Radimetrics dose reporting system, and the Electronic Medical Record. Quality control will include regular data verification and protocol compliance checks by the PI and research personnel. The PI will submit annual reports to the UC Davis IRB detailing the study progress and enrollment status.

Breach of confidentiality

Confidentiality will be protected through periodic assessment, as new study materials and communication methods among project staff develop. The PI will report any confidentiality breaches to the IRB using the standard Reportable New Information form

11) Withdrawal of Subjects

Subjects will be withdrawn from the study without their consent if:

- They do not follow the study rules or they no longer meet the requirements to be in the study
- The study is stopped by the researchers or sponsor
    - The investigators feel it is in the participants' best interest to discontinue participation. Such circumstances may include unanticipated discomfort and/or fatigue from laying on the scanner table and/or feelings of fear or anxiety related to staying in a confined space (e.g., the PET/CT scanner)

12) Risks to Subjects

May include:

- Discomfort and/or fatigue from laying on the scanner table
- Feelings of fear or anxiety related to staying in a confined space (e.g., the PET/CT scanner)
- Bruising and/or infection at the IV site
- Radiation Risks: This study involves a radiation exposure that is typical of other diagnostic tests using ionizing radiation. The amount of radiation exposure received in this study is below the levels that are thought to result in a significant risk of harmful effects.
- It is possible that EXPLORER PET/CT may detect false positive findings that may require further follow-up (clinical, imaging or surgical) with all the risks associated with these follow-up procedures. These risks range from minor risks to severe risks including death and permanent disabilities. In addition, a misinterpreted or missed findings may give false information to the subjects about their health status.
- Hypoglycemia from prolonged fasting.

13) Potential Benefits to Subjects

In general, we expect there to be no benefit to the subject. If any incidental finding will be detected, they will be managed as described above in section "Procedures

Involved" of this protocol.

14) Sharing of Results with Subjects

The results of this research will not be shared with subjects. However, if any incidental finding are detected, they will be managed as described above in section "Procedures Involved" of this protocol.

15) Prior Approvals

This study has been approved by the UC Davis Health Radiation Use Committee.

16) Provisions to Protect the Privacy Interests of Subjects

The research team member obtaining consent will meet with the candidate in a private setting and will dedicate sufficient time to explain the study procedures and answer any questions. It will be explained that participation is strictly voluntary and declining to participate will not affect them in any way. A HIPAA disclosure form will be signed by the subject to allow access to their medical records.

17) Compensation for Research-Related Injury

If a subject is injured as a result of being in this study, the University of California will provide the necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by the University or the study sponsor or may be billed to the subject's insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, the subject may contact the IRB Administration at (916) 703-9151 or HS-IRBAdmin@ucdavis.edu

18) Economic Burden to Subjects

Research participants will not be charged for their participation. In case of abnormal, missed, misinterpreted, or unclear findings, the participant may decide in agreement with their Primary Care Physician to further investigate and the cost of this will be borne by the participant and/or their insurance.

19) Review Requirements

Are there any contractual obligations or other considerations that require IRB review of this research, or review at intervals other than those requiredby the Common Rule or FDA? If yes, check box:

☐ Yes

☒ No

Title of research study: [1714742] EXPLORER PET/CT: Evaluation of Healthy Individuals from Racial/Ethnic Minority Populations

Investigators: Moon S. Chen, Jr., Ph.D., M.P.H., Professor; Lorenzo Nardo, M.D., Ph.D., Associate Professor

California Experimental Subjects Bill of Rights

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any drug or device to be used.
- Any common or important discomforts and risks.
- Any benefits you might expect.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document.

Key Information about This Research Study

You are invited to participate in a research study. The purpose of this research is to test the performance of a new Positron Emission Tomography/Computerized Tomography (PET/CT) scanner, which is a type of medical scanner. It is called EXPLORER and it is the first FDA-cleared medical scanner to be able to scan the entire human body at the same time. EXPLORER is much more efficient than previous PET/CT scanners and has the potential to make a big impact in medical care and research. You are invited to be in this study because you are a healthy volunteer who has expressed an interest in participating and you identify as a racial/ethnic minority.

Your participation in this research may involve up to two visits. The first visit (consenting and screening) will inform you of study details and determine your eligibility. During this visit you will be asked to sign an informed consent if you want to take part in the study before proceeding to the screening part. The other visit will involve the study scanning procedure which will last approximately 3 hours. We expect 20 people will participate in this research at UC Davis.

Participation in this study will involve PET/CT scans. For the PET/CT scan, you will be injected with a small amount of a radioactive sugar (called F-18 fluorodeoxyglucose, or FDG) and you will lay on your back inside a long PET/CT scanner (the EXPLORER scanner).

We will also ask you for a blood sample to use in doing studies of your ancestry. Some of the tests we will perform on your blood sample will be genetic testing, which is done on your DNA. DNA, or deoxyribonucleic acid, carries the genetic instructions for the cells that make up your body. Genes tell

your body how to do things like form your spine, or what color your eyes should be. In addition to taking the steps described in this document to protect the privacy of your genetic information, there is a Federal law called the Genetic Information Nondiscrimination Act (GINA) that prohibits employers and health insurers from discriminating against you on the basis of your genetic information. Another Federal law called the Affordable Care Act (ACA) prevents health insurers from denying insurance to people with pre-existing conditions, including genetic conditions. A California state law called CalGINA increases the protections of the Federal GINA law by also protecting you from being discriminated against on the basis of your genetic information by emergency medical services, housing agencies, businesses, lenders, or state-funded activities or programs.

All research studies involve some risk. These risks are described in detail later in this document. We do not expect that you will benefit from participation in this study. Here are some reasons you may not want to participate in this research. The scanning visit could last up to 3 hours. Avoiding strenuous exercise, the day before, and fasting for 6 hours prior to the PET/CT visits, may be undesirable. For some people lying inside the scanner may cause fear or anxiety due to the confined space, and/or discomfort. Also, the scan may reveal suspicious findings and/or findings of unclear cause which may need further follow-up procedure(s) or give you false reassurance about your health conditions. Medical follow-up may include doctor's visits, more scans or surgery and may expose you to additional risks from the follow-up procedure(s).

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions you need to help decide whether or not to join this study.

Information to help you understand research is online at
http://www.research.ucdavis.edu/policiescompliance/irb-admin/for-research-participants.

What if I have Questions?

The persons in charge of this study are Dr. Moon Chen and Dr. Lorenzo Nardo. If you have questions or concerns about this study, please contact the Study Coordinator at 916-731-9004 who will help you get in contact with Drs. Chen or Nardo.

For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to the Nuclear Medicine Physician on duty. In the case of an emergency, dial 911 from any phone.

If you have any questions about your rights as a research subject or have complaints about the research study or study team, you may talk to a team member at the Institutional Review Board (IRB) at (916) 703-9151, through email hs-irbadmin@ucdavis.edu, or at this address 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817. The IRB is a group of people who oversee research.

How is this research funded?
This research is being funded by the US National Institutes of Health (NIH) also called the sponsor. Sponsors may change or be added.

The University of California has a financial interest in this study. The University has granted a license to a private company to develop the device being tested in this study. If the device proves to be safe and effective, the University could financially benefit from the sales of the device.

Why is this research being done?
One specific gap with ongoing research out of the EXPLORER Molecular Imaging Center (EMIC) is the need to have "healthy" (non-cancer) participants. The aim of this pilot study is to increase the number of healthy individuals from racial/ethnic minority populations. This will advance research being conducted at EMIC by providing "controls" or comparisons to differentiate between images from patients with cancer versus healthy people of the same racial/ethnic ancestry. In addition, blood samples from participants to this study will be utilized for quantitative, genetics-based estimates of ancestry (e.g., African, Chinese, Colombian, Western European, Mexican, Vietnamese, etc.), which is especially valuable in the case of admixed individuals. In order to accomplish this, we will utilize the UCDCCC's Genomics Shared Resource (GSR) for Whole-exome sequencing (WES) and contemporary computational analyses.

What happens if I say yes, I want to be in this research?
If you decide to participate in this research study, the researchers will ask you to have up to 2 visits. If you decide to participate, you will be asked to do the following:

- On your first visit (consenting and screening).
  - This visit can be done over the phone/remotely or in person at the EXPLORER Molecular Imaging Center (EMIC), 3195 Folsom Boulevard in Sacramento.
  - The researcher will explain the study in detail. Then, if you want to participate, the researchers will ask you to sign a consent form.
  - After signing the consent form, you will be asked several questions in order to determine your eligibility for this study.
  - You can withdraw from this study at any time by letting anybody from the research team know.
  - You will be asked for phone number, email and postal address to contact you. A member of the research team will use this information to contact you for scheduling and to convey any study-related information to you.

- On your second visit, you will have a series of PET/CT scans:
  - The *day before* your PET/CT scans you will need to avoid any strenuous exercise or physical labor.
  - The *day of* your PET/CT scans, you will need to fast (not eat anything) for 6 hours prior to your scan. Drinking plenty of water is OK.

- You will need to avoid consuming any sugar in any form for 6 hours prior to your PET/CT scans. So, you need to avoid drinking soda or anything sweet. Drink water if you are thirsty.
- You will also need to avoid caffeine and nicotine for six hours prior to your PET/CT scans.
- On the day of your PET/CT scans, you will come to EMIC at 3195, Folsom Boulevard in Sacramento.
- A technologist will ask you some questions and/or give you some tests (to test blood sugar level and pregnancy if applicable) to make sure everything is OK for the PET scan.
- A urine pregnancy test will be administered at no charge to all participants who are able to get pregnant between 18 to 60 years old, unless documented hysterectomy or bilateral ovarian removal is available.
- Your blood sugar level will be measured with a needle-stick to make sure you do not have too high a blood sugar level for the study to work.
- Your height and weight will be measured.
- You will be asked to remove your clothing and wear a hospital gown that we will provide.
- You will have an IV needle placed in a vein for injection of 8-12 mCi of [18F]fluorodeoxyglucose (FDG), a radioactive sugar.
- Before the scans begin, you will have 3-5ml of blood (about a tablespoon) drawn through a needle from a vein in your arm for genetic ancestry testing.
- You will then receive a whole-body CT scan (quicker than 1 minute on the same scanner). This will be followed by a PET scan on the EXPLORER scanner lasting 60 minutes which starts when the radioactive sugar is injected.
- You can then get off the scanner, stretch, use the restroom, or rest in a quiet room at EMIC
- We will also ask you if you had any bowel movements after injection with FDG until you complete your scans.
- 90 minutes after your injection, you will have another 20-minute PET scan. This scan will be immediately preceded by a CT scan (quicker than 1 minute on the same scanner)
- 120 minutes after your injection, you will have another 20-minute PET scan. This scan will be immediately preceded by a CT scan (quicker than 1 minute on the same scanner)
- The total amount of time you will spend on this second visit is approximately 3 hours.

How is being in this study different from my regular health care?

If you take part in this study, the main difference between your regular care and the study is that your regular health care does not involve any procedures done in this study including PET/CT scans.

Do I have to be in this study? What if I say "yes" now and change my mind later?

No, you do not have to be in this study. Taking part in research is voluntary. You can choose to be in the study or not be in the study. If you decide to be in the study, you can choose to leave the study at any time.

If you decide not to take part in the study, or if you choose to leave the study, your choice will not affect any treatment relationship you have with healthcare providers at UC Davis Health or any services you receive from them. No matter what you decide, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

Please let the researchers know if you choose to leave the study.

If you stop being in the research, data that have already been collected will not be removed from the study database.

Can I be removed from the research without my OK?

The researchers may take you out of the study, even if you want to continue, if:

- you do not follow the study rules, or you no longer meet the requirements to be in the study
- the study is stopped by the sponsor or researchers.
- the investigators feel it is in your best interest to discontinue participation. Such circumstances may include unanticipated discomfort and/or fatigue from laying on the scanner table, and feelings of fear or anxiety related to staying in a confined space in the scanner

Is there anyway being in this study could be bad for me?

There are risks to participating in this research. The study doctor and study team will monitor you to see if you are experiencing any harm related to your participation. If you experience any pain or discomfort, you must inform the study team as soon as possible.

Radiation risks: This study involves a radiation exposure that is typical of other diagnostic tests using ionizing radiation. The amount of radiation exposure received in this study is below the levels that are thought to result in a significant risk of harmful effects.

You are exposed to radiation on a daily basis, both from natural (sun and earth) and manmade sources. The estimated radiation dose that you will receive as a participant for this type of research has been compared to the limits allowed for a radiation worker. This limit is low and is not expected to be harmful. The person obtaining your consent can answer any questions you have and provide detailed written information about the amount of radiation resulting from this study.

PET scans involve the risks of radiation (see above). If you have had a PET scan or have been exposed to radiation while participating in other research during the past year, you should inform the researcher(s). This will enable the researcher(s) to determine your total radiation exposure and make sure it does not exceed accepted safety guidelines. If you participate in future studies that involve the use of X-rays or radioisotopes, you should discuss the safety guidelines for radiation exposure with the researcher who is performing the study.

Risk of the Radiotracer (18F-FDG): A side effect from Fludeoxyglucose F18 Injections is uncommon. Side effects include allergic reactions, itching, rash, and water retention. To minimize radiation exposure to your bladder, you should drink at least an 8 oz glass of water before injection with the radiotracer and after your PET/CT scans. To help protect yourself and others, you should flush the toilet several times after each use for 12 hours after injection with the radiotracer. You should also wash your hands after

each use of the bathroom. If your blood, urine, or feces come in contact with your clothing, you should wash them separately from other clothes.

Minor risks:

- Blood draw risks: Blood draws may cause temporary discomfort from the needle stick, bruising and, rarely infection and fainting. If more than one unit of blood is to be drawn within an 8-week period, a medically appropriate precaution concerning subsequent blood donation is required
- Bruising or infection at the site of the injection.
- Discomfort from lying on the scanner table multiple times for up to 60 min.
- Feelings of fear or anxiety related to staying in a confined space
- There is risk for having low blood glucose because of prolonged fasting.

There is a possibility that the scan(s) will reveal some suspicious findings or findings of unknown cause, that may require further medical follow-up. If this is the case, your doctor will be notified within 8 weeks, or immediately if the finding indicates an urgent nature. This is discussed further on page 7 of this consent. As with all research, there is a chance that confidentiality could be compromised; that is, that your information could become known to someone not involved in this study. To minimize the risks of breach of confidentiality, we will include information that directly identifies you only during the acquisition and storage of data including encrypted external password protected hard-driver and the UC Davis PACS system. PACS refers to Picture Archiving and Communication System, which consists of multiple machines, computers, and/or devices connected together for easy access to huge number of medical images. However, any information that directly identifies you will not be shown in publications, talks or any other presentations about this research.

What about Birth Control?

Contraception Requirements for Women

The study involves radiation that may harm a fetus or a breastfeeding baby. If you are pregnant or breastfeeding, you cannot take part in this study. If you think you may be pregnant, you should not volunteer for this study. A urine pregnancy test will be administered at no charge to all participants who are able to get pregnant between 18 to 60 years old, unless documented hysterectomy or bilateral ovarian removal is available.

Will being in this study help me in any way?

Being in this study will not help you directly. But your participation in the study may benefit other people in the future by helping us learn more about this new scanner. This study is not a substitute for your regular medical care. You should continue to see your regular medical providers.

Will being in this study cost me anything?

There will be no cost to you for any of the study activities or procedures. You will have to pay for basic expenses like any childcare, parking, or transportation related to study activities.
If you need further medical follow-up procedures (which may include doctor's visits, more scans or surgery) because of the study findings, you or your insurance will need to pay for that.

For more information about possible costs, please contact the research team. The research team can follow UC Davis Uninsured Non-Emergency Estimate Policy (Policy ID 1883) to work with their department and Decision Support Services to get you a cost estimate.

Will I be paid or receive anything for being in this study?

We will pay you up to a maximum total of $100 for participating in this study. We will pay you $25 for being injected with the radiotracer (18F-FDG, which is the most widely used dye in PET examinations), plus $25 for each hour you spend in the study.

Payment will be provided in the form of gift card(s). If you choose to leave or we take you off the study before you complete the study visit, your payment will be pro-rated according to the hours spent per studies (one hour = $25). Please note that there is no compensation for the initial consenting and screening visit. Also any optional visit to talk with a study doctor about any findings there may be from the tests and/or scans will not be compensated.

Biospecimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

What happens if I am injured or get sick because of this study?

If you are injured or get sick because of this study, medical care is available to you through UC Davis Health, your local provider, or emergency services.

- If it is an emergency, call 911 right away or go to the emergency room.
- For non-emergency issues, you can call the UC Davis Health Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to nuclear medicine radiologist on-call.

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide the necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by the University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may contact the IRB Administration at (916) 703-9151 or HS-IRBAdmin@ucdavis.edu.
If the sponsor pays any of your medical expenses, we may be required to give the sponsor your name, date of birth, and Medicare ID or social security number.

What happens to the information collected for the research?

We will do our best to limit the use or disclosure of your personal information, including information from this research study and from your medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Some organizations may be required to inspect and copy your information including the IRB and other University of California representatives responsible for the management or oversight of this study.

We have strict rules to protect your personal information and protected health information (PHI). We will limit who has access to your name, address, phone number, and other information that can identify you.

At the time of collection of data, your identifiable information will be entered into the system database.

The PET/CT images created for this study are for research and are not meant to judge the level of your health, as they would be if they were part of your medical care. The images will not receive the usual clinical review by radiologists who interpret PET/CT scans. This means that some findings may be overlooked or misinterpreted. However, if a member of the study team, while reviewing your images, notices any findings they will share this with the Study Radiologist. If the Study Radiologist thinks a medical problem might be present, we will contact you within 8 weeks to discuss the possible medical problems or immediately if it appears urgent to the Study Radiologist. If you request it in writing, we can provide you with a copy of a section of your CT and PET images to take to a doctor you designate. We may not be able to share any images from the PET portion of your scan if they are difficult to interpret or if we are restricted by the sponsor of the study. We will send a letter to a doctor you designate letting them know that you are enrolled in this study and that it included getting a PET/CT scan for research. The letter will also state that the images did not receive the usual clinical review but that findings related to a possible medical problem were seen by a UC Davis radiologist. We will also provide the doctor you designate with a copy of your radiology report. Your doctor can contact the Study Radiologist, Lorenzo Nardo MD, at any time to discuss your PET/CT scan. In addition, there is a possibility that Dr. Nardo or a designee may contact you to ask if you received any sort of medical follow up.

Before this data is analyzed for our research, we will remove identifiable information from all the data. After we remove all of the identifiers, we will place a code on the information. The code will be linked to your identity, but the link will be kept in a location that is separate from your study data. We will maintain your study data on encrypted password-protected computers and/or devices and access to the information will be limited to only members of the research team who need the access to properly conduct the study. In addition, your data with identifiable information will be kept in the UC Davis Radiology Picture Archiving and Communication System (PACS). The information we send to the sponsor will not include information that directly identifies you.

While this study does involve banking the data we collect with your identifiable information (e.g., your name, medical record number, or date of birth) for future use, we may still use your data to answer additional research questions or share them with other investigators for additional research. If we do so,

we will remove all identifiable information before use or sharing. Once identifiers have been removed, we will not ask your consent for the use of sharing of your data in additional research.

However, we cannot promise complete confidentiality. If you agree to be in this study, Federal or state laws may permit or require us to show information to university or government officials and to study sponsors responsible for monitoring this study. We may also show your medical records to study monitors, auditors, the IRB, and the FDA. These groups are obligated to maintain your confidentiality. The following is a list of individuals who may access your records:

- Members of the research team
- Offices and committees responsible for the oversight of research
- Personnel who schedule or perform medical tests or procedures, handle accounting and billing, or do other tasks related to this study
- Your Primary Care Physician
- U.S. Office for Human Research Protections
- The study sponsor, the US National Institutes of Health
- Collaborating researchers outside of UC Davis, after obtaining regulatory approvals
- Companies or groups performing services for the research team, such as Northern California PET imaging center staff

If you agree to participate in this research study, a signed copy of this consent document will be filed in your electronic medical record (EMR) to ensure people caring for you at UC Davis Health will have the information they need about this research study when they provide care for you. In addition, some of your images will be stored in the UC Davis clinical image database known as Picture Archiving and Communication System, and a report detailing your radiation dose will be stored in the UC Davis dose reporting system

We will access protected health information (e.g., your medical record) for this study and you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your medical records may be looked at by the sponsor of this study and government agencies or other groups associated with the study. They may not copy or take your personal health information from your medical records unless permitted or required by law.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/legal/privacy/) and in an attached document.

Biological specimens (urine and blood sample) are used only for screening purpose. After the results are recorded the biological specimens will be discarded.

This research is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. The researchers with this CoC may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding. For example, the information collected in this research cannot be used as evidence in

a proceeding unless you consent to this use. Information, documents, or biospecimens protected by this CoC cannot be disclosed to anyone else who is not connected with the research, except:

- To a federal agency sponsoring this research when information is needed for auditing or program evaluations;
- To meet the requirements of the U.S. FDA;
- If a federal, state or local law requires disclosure such as a requirement to report a communicable disease;
- If information about you must be disclosed to prevent serious harm to yourself or others such as child abuse, elder abuse or spousal abuse;
- If you consent to the disclosure, including for your medical treatment, to an insurer or employer to obtain information about you; or
- If it is used for other scientific research, as allowed by federal regulations protecting research subjects.

This CoC also does not prevent you or a family member from voluntarily releasing information about yourself and your involvement in this research.

Will I receive any results from this research?

We will create a radiation dose report from your PET/CT scans and we will give you a copy if you ask for it.

The results of this research will not be shared with you. However, you and your primary care doctor will be notified if any incidental findings are detected as described above in the section "What happens to the information collected for the research?" of this informed consent form.

To be part of this study, you need to have a Primary Care Physician and health insurance. You will need to provide contact information for you and for your Primary Care Physician.

Will information or leftover specimens be used for other research?

During this research, the study team will obtain information about you. They will also collect biological specimens from you such as blood (to check your blood glucose level and to conduct ancestry studies) or urine (pregnancy test). The data will be used for this research while the specimens will be thrown away.

May we contact you by phone and/or e-mail?

To be part of the study, we need your phone number, mailing address and email address (if you have one) so we can communicate with you for any matter related to this study including your scheduled visits. Phone number is generally a more direct and faster way to communicate and it will be always preferred in case there will be the need of an immediate or urgent intervention based on the results of your scans and/or tests. Email is generally not a secure way to communicate about your health, as there are many ways for unauthorized users to access email. You should avoid sending sensitive, detailed

personal information by email. Email should also not be used to convey information of an urgent nature; however, it may be used to communicate non-urgent matter.

If you need to talk to someone immediately, please contact the Study Coordinator, 916-731-9004.

Please provide your contact information here:

Phone: _____

E-mail : _____

Mailing address:

Apartment Number: _____

Street address: _____

City: _____

State: _____

Postal code: _____

Country: _____

What are my rights when providing electronic consent?

- California law provides specific rights when you are asked to provide electronic consent:
  - You have the right to obtain a copy of the consent document in a non-electronic format.
  - You have the right to provide consent in a non-electronic format.
  - If you change your mind about electronic consent, you have the right to request your electronic consent to be withdrawn and you can then provide consent in a non-electronic format; however, a copy of your electronic consent will be maintained for regulatory purposes. If you wish to withdraw your electronic consent, please tell the study team.
- This agreement for electronic consent applies only to your consent to participate in this research study.

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

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

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

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