INFORMED CONSENT DOCUMENT

Project Title: Frailty and Brain Integrity in Older HIV-Infected Individuals

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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 as a research participant. By signing this form you are agreeing to participate in this study.

- If you have any questions about anything in this form, you should ask the research team for more information.
- 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 are a person 50 years of age or older who has been infected with HIV.

The purpose of this research study is to study:
1. the effect of HIV on cognitive ability/brain functioning;
2. if older HIV-infected individuals with a combination of cognitive impairment and frailty are more vulnerable than those with one or the other; and
3. if frailty correlates with neuroimaging biomarkers of brain integrity in older HIV-infected individuals.

WHAT WILL HAPPEN DURING THIS STUDY?
To be eligible for the study:
- you must have a documented history of HIV infection
- your HIV must be well-controlled on stable cART regimens for approximately 3-6 months prior to enrollment
- you must be able to have an MRI.
For all participants, to determine your eligibility, you will have a screening evaluation, which includes:

1. Urine pregnancy test (done on the day of the scan and only for females with no documented history of sterilization, menopause, etc.)

2. A urine drug screening test for cocaine, amphetamines, methamphetamine, barbituates, benzodiazepines, marijuana, opiates, PCP, methadone, and tricyclic antidepressants (done on the day of the scan). A positive result will not necessarily exclude you from the study.

3. The Neuroimaging Screening Form, which asks questions about your feelings about being inside a closed space like the MRI scanner, questions about history of head injuries, and questions about any metal that subjects may have implanted in your body or any metal piercings that cannot be removed. This takes approximately 5 minutes to complete.

4. A Locator Form with your basic contact information, as well as additional names of people who might also be able to contact you should you be lost to follow up.

5. An assessment of frailty.

6. You will be asked questions about your demographics and other basic information, such as age, race, gender, handedness, years of education, first language, height/weight, date of HIV diagnosis (and date started medications if applicable), as well as information about drug, alcohol, tobacco and caffeine use.

7. You will also be asked to sign a Release of Information form so we can obtain your medical records, including but not limited to medical, hospitalization, HIV, STD, substance use/abuse/dependence and mental health records from your doctors, results from prior blood, diagnostic, imaging and laboratory tests and other information obtained from interviews or questionnaires related to your medical care. We may also review the records of any Washington University research study in which you participate. This will allow us to better determine your eligibility, insure and improve your safety, and decrease your burden if the results of tests done in one research study could be used as data for another instead of asking you to unnecessarily repeat a procedure.

8. We will review your medical history and records related to any of your HIV/AIDS-related outpatient visits, inpatient hospitalizations, blood/diagnostic/laboratory/imaging tests (such as CD4 count, viral load, nadir CD4 count, duration of infection, thyroid and liver function, creatinine, c-reactive protein, complete blood counts studies, total fasting cholesterol with LDL/HDL and triglycerides, fasting glucose, and glycosylated hemoglobin, STD history, AST, ALT, fibrinogen-4, GFR, platelets, HCV, IL-6, d-dimer, hsCRP, and any other HIV- or inflammatory-related labs deemed necessary; any abnormal/exclusionary imaging results, etc.), substance use/abuse/dependence, and mental health treatment. Additional information may also be obtained from clinical interviews or questionnaires found in your records related to your medical care. We may also review your research records from other WUSM studies (to see if previous results indicate any exclusionary criteria or provide any results.
that we could use as data for this study so as to not have you repeat procedures and decreasing your burden whenever possible). These records will only be accessed as long as necessary to acquire study data.

9. Blood draw: If we cannot acquire records of labs listed in #8 having been drawn in approximately the past 12 months, we may draw them at this time or on the day of the MRI/neuropsych testing (described below). The blood draw will be done by staff of either the ACTU, ID Clinic, Barnes or Quest Laboratory, or the Center for Clinical Studies (CCS) and will be equivalent to approximately 4 tablespoons. This amount of blood will only be drawn from you now and when you return for your follow-up visit (see below).

If, on the basis of these tests and at the PI’s discretion, you are found to be eligible for the study, you will be asked to complete the following study procedures. When you come for these evaluations, we ask that you refrain from eating or drinking anything besides water for approximately 8 hours prior to the scan, do not have any caffeine for approximately 5 hours, and do not smoke or chew tobacco for approximately one hour.

1. Neuropsychological (Memory) Tests -- These are exercises that are related to memory, how fast you do things with your hands, and how you pay attention to tasks. There are a number of different tasks; some are timed and some are not. These will take approximately 1 hour to complete.

2. Questionnaires regarding your mood, ability to care for yourself, as well as your drug and alcohol history. These will take approximately ½-1 hour to complete, and you may skip any questions that make you feel uncomfortable.

3. MRI -- The MRI scanner is a powerful magnet that uses simple radio waves to take pictures of your brain. There is no pain associated with this procedure. You will be positioned on your back on the scanner bed and made to feel as comfortable as possible. The scanner bed will be moved inside a large tube so that your head and your chest are inside, but you will be able to see out into the room by your feet. During the scan, you will hear loud, rhythmic knocking sounds. Your ears will be covered to keep the noise at a minimum. There is a speaker and a microphone in the scanner so that you can talk to the MRI technician if there is something you need. Once the scan starts, you will need to lie still since moving around will interfere with taking pictures of your brain. You will be able to end the scan at any time if you feel uncomfortable. You may be asked to do a task while in the scanner. The MRI will take approximately 1 hour to complete.

4. Neuromedical examination -- A doctor will examine the nerves in your face, as well as test your reaction to touch and will test the reflexes in your arms and legs. We will check your waist circumference. This will take approximately 10 minutes.

5. We may also review your medical history and records including any physical exam reports, laboratory and imaging results.
In approximately 2-3 years, we will ask you to return for a follow up visit to repeat these same screening and testing procedures again. This will allow us to see if there has been any change in your brain’s structure and function over time.

6. APOE testing: Approximately 3 tablespoons of blood will be drawn at either your baseline or follow-up visit in approximately 2-3 years to determine if you are a carrier of the Apolipoprotein E (ApoE) ε4 allele. This is a genetic test to help further our understanding of HIV-related dementia (memory loss and thinking problems) and other neurodegenerative disorders (neurodegeneration refers to the progressive loss of structure or function of nerve cells). Some versions of this allele may increase a person’s risk of developing Alzheimer’s disease in their lifetime. This test is for research purposes only and its result will not be reported to you or your physician.

Will you save my samples or research data to use in future research studies?
As part of this study, we are obtaining neuroimaging, neuropsychological, and laboratory data from you. By agreeing to be part of this study you give up any property rights you may have in the neuroimaging, neuropsychological, and laboratory data. We would like to use your neuroimaging, neuropsychological, and laboratory data for other research projects in the future. These future studies may provide additional information that will be helpful in understanding HIV/AIDS, memory, thinking, aging, and various neurodegenerative disorders (i.e., Alzheimer’s Disease, HIV-Associated Neurodegenerative Disease, Multiple Sclerosis, other types of dementia, etc.), but it is unlikely that what we learn from these studies will have a direct benefit to you. It is possible that your neuroimaging, neuropsychological, and laboratory data might be used to develop tests, treatments or cures. There are no plans to provide financial compensation to you should this occur. If you agree, this means we will store your neuroimaging, neuropsychological, and laboratory data and may use it for studies going on right now as well as studies that are conducted in the future, and that the data we collect from your participation in this study may also be analyzed alone or with data gathered in other, separate studies.

We would also like your permission to share your neuroimaging, neuropsychological, and laboratory data with other investigators doing research in similar fields such as HIV/AIDS, memory, thinking, aging, and various neurodegenerative disorders (i.e., Alzheimer’s Disease, HIV-Associated Neurodegenerative Disease, Multiple Sclerosis, other types of dementia, etc.). These investigators may be at Washington University or at other research centers. We may also share you research data with large data repositories (a repository is a database of information) for broad sharing with the research community. If your individual research data is placed in one of these repositories only qualified researchers, who have received prior approval from individuals that monitor the use of the data, will be able to look at your information.

Your neuroimaging, neuropsychological, and laboratory data will be stored without your name or any other kind of link that would enable us to identify which sample(s) or data are yours, and if we share any of your data with other investigators, the information will be sent by coded ID#. Therefore, if you give permission to store and use your neuroimaging, neuropsychological, and laboratory data it will be
available for use in future research studies indefinitely and cannot be removed.

Any genetic samples taken for APOE testing, however, will be destroyed at the conclusion of the study.

HOW MANY PEOPLE WILL PARTICIPATE?
Approximately 250 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 involvement will last for approximately 4-5 hours (screening visit, lasting approximately 1-1½ hour, plus MRI/neuropsych testing visit, lasting approximately 3 hours). Depending on scheduling availability and your preference, these tests may be scheduled all on one day or split into 2 visits. We will then ask you to return and repeat these same procedures in approximately 2-3 years.

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.

RISK OF THE FRAILTY SCREENING, NEUROPSYCHOLOGICAL (MEMORY) TESTS, & QUESTIONNAIRES
Likely: None

Less Likely:
- You may feel embarrassed or uncomfortable answering some of the questions.
- You may experience fatigue or embarrassment from the exercises of memory, movement, and attention.
  You may discuss any question that concerns you with the coordinator, and you may choose not to answer any question that makes you feel uncomfortable.

Rare: None

RISKS of MRI
Some things may interfere with Magnetic Resonance Imaging (MRI), and some can be potentially dangerous. You should inform the study doctor if you have any of the following:
- Heart problems
- Pacemaker
- Metal implanted under your skin, such as an insulin pump
- Hearing aid or cochlear implant
- Surgical clips or staples
- Any metal prosthesis. A prosthesis is an artificial body part, like an artificial leg.
- Shrapnel of bullet
• Tattooed eyeliner
• Metal dental items
• Braces
• Pregnancy

**Likely:**
**Metal in or on the body**
The MRI scanner functions like a magnet and any metals in your body can be pulled off by the machine. If you have metal implants (under the skin) such as a pacemaker or metal pins or rods) you may be at risk when you are close to the machine. To minimize this risk, we will ask you a series of questions about metal exposure over the course of your lifetime from work experiences and medical procedures.

**Claustrophobia (fear of small spaces)**
When you have the MRI you will lie on a small bed and the bed will be inserted inside a large tube. The opening of the tube is narrow, and some people can experience claustrophobia (anxiety or nervousness while inside small spaces) when in the scanner. If you believe that you may experience anxiety or nervousness while inside the scanner you should not participate in this study. If you decide to participate in the study and begin to experience claustrophobia while inside the scanner, we will immediately stop the procedure at your request.

**Body Stiffness**
You may also experience stiffness from lying still for a long time while in the scanner.

**Less Likely:** The scanner produces a loud repeating knocking noise during the scan that some people find bothersome. To lessen the noise, you will be given head phones.

**Rare:**
• Occasionally, some people may experience a short period of dizziness or feel faint after being in the scanner.
• There is a rare possibility that a serious abnormality may be discovered by the technician during the MRI picture of your brain. In this event, you will be referred to your primary care physician and/or the WUSM Neurology Clinic for clinical follow up and treatment as appropriate.

**RISKS ASSOCIATED WITH BLOOD DRAW**
**Likely:** Pain at the site of needle insertion.

**Less Likely:** none

**Rare:** Infection at the site.

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

**WHAT ARE THE BENEFITS OF THIS STUDY?**
You will not receive any direct benefit from this study. However, we anticipate that this study will provide valuable data to facilitate our understanding of the relationship between physical frailty and neurocognitive impairment in older HIV+ participants and may help future adjunctive therapies. While this is not a treatment study and will not affect disease status, those engaged in the research will receive free neuroimaging (albeit not for clinical purposes) and evaluations of physical frailty and neurocognitive impairment that will far surpass the general standard of practice.

**WHAT OTHER OPTIONS ARE THERE?**
There are no other options to participation in the study.

**WILL IT COST ME ANYTHING TO BE IN THIS STUDY?**
You will not have any costs for being in this research study.

**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 so that a check can be mailed to you. The check will be requested after your complete the study, but it may take about 2 weeks for you to receive it. If your social security number is obtained for payment purposes only, it will not be retained for research purposes.

The total amount of compensation for being in the study will be up to $125.00:
- $10 for screening
- $15 for screening labs (if they have not completed within approximately the past 12 months) and/or APOE testing
- $100 for MRI, neuromedical exam, neuropsychological (NP) testing, and questionnaires.

You will be paid only if you qualify and complete the MRI and all neuropsychological testing and questionnaires.

**WHO IS FUNDING THIS STUDY?**
The National Institute of Health (NIH) is funding this research study. This means that Washington University is receiving payments from NIH 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 NIH 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 the investigator (Dr. Beau Ances at 314/747-8423) and/or the Human Research Protection Office at 314/633-7400 or 1/800/438-0445.
Decisions about payment for medical treatment for injuries relating to your participation in research will be made by Washington University and NIH. 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?**

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.
- NIH
- University representatives, to complete University responsibilities
- Washington University’s Institutional Review Board (a committee that reviews and approves research studies)
- Public health agencies to complete public health reporting requirements
- Your primary care physician if a medical condition that needs urgent attention is discovered.

To help protect your confidentiality, we will keep all information in a locked area. The information you give us will be given a code number. A master list linking the code number and your identity will be kept separate from the research data. Only the Principal Investigator and people helping him will be able to see the list, and all staff involved with this project have been thoroughly trained in the protection of research participants. We will protect your information, but there is a chance somebody might see it.

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.

Some of the individual results from tests to be performed during this research study might be of interest to you or your primary care physician. At your request, the researchers will share the medical information gained from this study with you and your referring and/or primary care doctors. If we discover significant abnormal test results or an urgent medical condition that requires treatment, we will notify your primary care physician for your health and safety even if you don’t request that we do.

We will also share de-identified data with colleagues at the University of California Los Angeles.

To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS). This Certificate may prevent the researcher from being forced (for example by court subpoena) to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding. However, a Certificate of Confidentiality does not prohibit the researcher from disclosing information about you or your involvement in this research that you have agreed to disclose or make available. For example, if you or your legally authorized representative request in writing that
information about you or your participation in the research be released to an insurance company, the researcher may not use the Certificate of Confidentiality to withhold this information. This means that you and your family should actively protect your own privacy. Finally, the researcher is not prevented from taking steps, including reporting to appropriate authorities, to prevent child abuse or serious harm to yourself or others.

**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. 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.

**WILL YOU KEEP MY NAME ON FILE TO GIVE TO OTHERS?**

We will keep information about you in a special kind of computer listing called a registry. A registry keeps information about you on file so that other researchers, not involved in this particular study, may contact you in the future about whether you are interested in being in different research studies. The registry will contain information such as your name, address, age, and selected medical information such as diagnosis and treatment. We will keep the information in this registry secure by keeping an electronic document with this information password protected, saved on a password protected computer, and by keeping a paper copy of this information behind two locks, in compliance with WUSM regulations. You may request that your personal information be removed from this file at any time by contacting Elizabeth Westerhaus at 314/747-1125.

Being in the registry is optional (i.e., you can still enroll in this study even if you don’t want to be placed in the registry). You can tell us your choice by initialing in the appropriate spot below.
I give you permission to put my name and personal information in a registry so that other researchers can contact me in the future about different research studies.

_____ Yes  _____ No
Initials  Initials

You can refuse to participate in any study offered to you or request to never be contacted for future studies again.

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
- Your signature and this form will not expire as long as you wish to participate.
- 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 [http://hrpo.wustl.edu](http://hrpo.wustl.edu) (or use the direct link: [http://hrpohome.wustl.edu/participants/WithdrawalTemplate.rtf](http://hrpohome.wustl.edu/participants/WithdrawalTemplate.rtf)) 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 if necessary 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. 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 [http://hrpo.wustl.edu](http://hrpo.wustl.edu) under Information for Research Participants.

There will be no adverse consequences or changes to your insurance or health care if you choose to no longer participate in the 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 because if you have certain medical conditions like seizures, use of illegal drugs, or pregnancy or because in our judgment it would not be safe for you to continue, or because the funding for the research study has ended.

WHAT IF I HAVE QUESTIONS?
We encourage you to ask questions. If you have any questions about the research study itself, please contact: Elizabeth Westerhaus at 314/747-1125 or Dr. Beau Ances at 314/747-8423. If you feel that you have been harmed in any way by your participation in this study, please contact Dr. Beau Ances at 314/747-8423.

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, (314) 633-7400, or 1-(800)-438-0445 or email hrpo@wusm.wustl.edu. General information about being a research participant can be found by clicking “Participants” on the Human Research Protection Office web site, http://hrpohome.wustl.edu. To offer input about your experiences as a research subject 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.

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: 11/21/14.**

__________________________________________ _______________________________
(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 he or she understands 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)