Biodistribution of [11C]Acetoacetate/[18F]Fluorodeoxyglucose in Subjects With Risk Factors for Alzheimer's Disease (AcAc PET)

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DEPARTMENT OF RADIOLOGY AND NEUROSURGERY
DEPARTMENT/SECTION OF INTERNAL MEDICINE/GERONTOLOGY & GERIATRIC MEDICINE
ROENA B. KULYNYCH CENTER FOR MEMORY AND COGNITION RESEARCH

Biodistribution of [11C]Acetoacetate/[18F]Fluorodeoxyglucose in Subjects with varying Risk Factors for Alzheimer's disease and Subjects on a Diet Intervention

Informed Consent Form to Participate in Research
Suzanne Craft PhD, Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to identify and measure the amount of glucose or sugar and ketone body metabolism in your brain using experimental radioactive compounds called [11C]AcAc and [18F]FDG. Glucose metabolism in other parts of the body will also be measured. You are invited to be in this study because you are enrolled in the Wake Forest Alzheimer's Disease Clinical Core (WFADCC) or an affiliated study such as BEAT-AD. Your participation in this research will involve 3 visits and last between 4 and 12 months.

Participation in this study will involve risks to you. All research studies involve some risks. A risk to this study that you should be aware of is exposure to radiation associated with the PET scanner. Additional information related to this risk is listed below. There are no benefits to you from participation in this study.

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. Some other choices may include not to participate and continue with your standard care. 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 if you need help deciding whether to join the study. The person in charge of this study is Suzanne Craft, PhD. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in this research study because you are enrolled in the Wake Forest Alzheimer's Disease Clinical Core (WFADCC) or an affiliated study such as BEAT-AD. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to have a PET scan (Positron Emission Tomography), for a research study called the Biodistribution of [11C]Acetoacetate/[18F]Fluorodeoxyglucose in Subjects with varying Risk Factors for Alzheimer's disease and Subjects on a Diet Intervention. This consent form describes what you may expect if you decide to participate. Your participation is voluntary. You are encouraged to read this consent form carefully and to ask your study doctor or the study staff to explain any words or information that you do not understand before making your decision whether or not to participate. You may also discuss the study with your friends and family. Please take your time in making your decision as to whether or not you wish to participate.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to identify and measure the amount of glucose and ketone body metabolism in your brain using experimental radioactive compounds called [11C]AcAc and [18F]FDG. How the brain utilizes energy is altered in Alzheimer's disease (AD) and related disorders. Research studies suggest that this change in brain energy usage can occur prior to disease diagnosis and that brain energy metabolism may be modified due to various interventions. Since changes in glucose metabolism may also occur in other parts of the body in people with AD, we will utilize [18F]FDG to measure energy usage in non-brain regions as well, including the chest, abdomen, and thigh.

The data collected in this study will help provide a more comprehensive understanding of brain energy metabolism (both glucose and ketone bodies) and non-brain energy metabolism (glucose only) in several groups of participants including adults with and without signs of memory impairment. The information collected will help us find out who is more likely to have changes in energy usage throughout the body, how this may be modified and how this relates to the risk for developing memory problems.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Up to 60 participants between the ages of 50-85 years will take part in this study at Wake Forest Baptist Medical Center. The total number of participants across all three groups will be 60. Participants will be from one of three groups:

Group 1: This group will include up to 10 healthy volunteers with no apparent memory problems, memory complaints or family history of Alzheimer's disease or dementia. Family history should include siblings, children and parents. Group 1 will complete 2 brain scan sessions in this study.

Group 2: This group will include up to 10 volunteers with pre-diabetes, but no apparent memory problems that can be observed during cognitive testing. Group 2 will complete 2 brain scan sessions in this study.

Group 3: This group will include up to 40 volunteers who have mild memory problems that are observed during cognitive testing. Group 3 will complete up to 2 brain scan sessions in this study.

WHAT IS INVOLVED IN THE STUDY?

Brain ketone body and glucose metabolism will be measured using PET with [11C]AcAc and [18F]FDG. Your participation will involve a maximum of two [11C]AcAc/[18F]FDG brain scans and a maximum of two whole-body [18F]FDG-PET/CT scans over the course of this study. We will collect your vital signs during visits 2 and 3.

STUDY VISITS?

Participants in groups 1, 2 and 3 will undergo all study visits over a period of up to 12 months. Groups 1 and 2 will complete the brain scans about 12 months apart. Group 3 will complete the brain scans about 4 months apart after a diet intervention.

CONSENT VISIT (VISIT 1)

During this visit, we will review this consent form with you and answer any questions you may have. You will not be considered eligible until you have signed this consent form. This visit will take approximately 30 minutes to complete.

BRAIN SCAN #1 (VISIT 2)

You will be asked to go to the ground floor of the MRI building to the Molecular Imaging Research PET/CT scanner at Wake Forest Baptist Medical Center.

- After your arrival, you will have a small catheter (plastic tubing with a needle on the end) inserted into a vein in both of your arms.
- Vital signs (blood pressure, heart rate, temperature) and body weight will be measured within 30 minutes of AcAc injection.
- A heating pad will be wrapped around one arm and up to 10 ml of blood will be drawn for metabolic measures.
- The [11C]AcAc will be injected into the catheter.
- After injection, the first part of the scan will begin immediately.
- Approximately 30-60 minutes after injection your body will begin to eliminate the AcAc compound.
- The [18F]FDG will be injected into the catheter.
- After injection, the second part of the scan will begin immediately.
- Blood will be sampled for laboratory testing through one of the arm catheters throughout each part of the scan.
- You will be positioned in the PET/CT scanner by trained staff and monitored throughout the scan with an audio microphone and video.
- During the scan, you must remain as still as possible. Before each PET scan session you will have a computerized x-ray (CT scan) to help align the positioning of your head.
- Brain PET/CT images will be acquired for a total of 90 minutes. A whole body PET/CT scan will be acquired for an additional 15-20 minutes. We have blankets and pillows available to help keep you comfortable. This visit will take about 3 hours to complete. You should not receive research PET/CT scans if you are pregnant or if you have received radiation therapy. Study staff will contact you 24-72 hours after your visit to discuss how you're feeling. You will not receive the results from this scan unless so indicated by a clinically significant medical finding.

BRAIN SCAN #2 (VISIT 3)
This visit will take approximately 3 hours to complete. Visit 3 includes the procedures listed in Visit 2 (described above).

HOW LONG WILL I BE IN THE STUDY?
Groups 1-2 will be in the study for twelve months. Group 3 will be in the study for about four months.

WHAT ARE THE RISKS OF THE STUDY?
Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the procedures we are studying include:

You will need to lie still for 110 minutes during the scan, which could be uncomfortable. There is a chance you may feel claustrophobic (afraid of small spaces) during your PET scan.

Radiation Exposure/Tracer Injection: This study involves exposure to radiation from the PET/CT scans. PET imaging involves exposure to small amounts of ionizing radiation, which has no expected harmful effects in the doses used for this purpose. However, the possibility exists for a rare reaction to any of the substances or procedures to which you are exposed. Because [11C]AcAc/[18F]FDG will be given in very small (trace) amounts, there are no additional drug-related risks associated with [11C]AcAc/[18F]FDG. There have been no adverse effects reported with the use of [11C]AcAc/[18F]FDG in previous studies using these tracers. PET/CT imaging involves exposure to small amounts of radiation. The effect of radiation on humans is measured in terms of Roentgen equivalents, or "rem." This is a unit of body radiation exposure. You will receive radiation from a "low dose" computed tomography (CT) scan, which is used to help align the positioning of your head in PET scans. The total dose of radiation from each combined PET/CT scan will be approximately 1.305 rem. The radiation dose you will receive from all PET/CT scans over the course of this 6 month study is equal to a dose of 3.61 rem, which is equal to about 72% of the yearly radiation exposure limit allowed for a radiation worker (5rem). The risk from this radiation exposure is considered to be comparable to other every day risks.

Blood Draws: A needle will be used to inject [11C]AcAc/[18F]FDG and blood sampling from a vein in your arm. Removal of blood by a needle and syringe poses a small and temporary risk of pain or bruising at the site of the needle stick. Some people may experience faintness or dizziness, and there is also a slight risk of infection at the site of the needle stick. To minimize these risks, experienced medical personnel will handle all the blood drawing procedures and sterile conditions will be maintained.

Reproductive Risks and other Issues to Participating in Research:
Due to unknown risks and potential harm to an unborn fetus from a PET scan, women who are not post-menopausal are excluded from participating in this study. If you are not post- menopausal or if you are pregnant, please let the study staff know. Each female participant of child bearing potential must affirm in writing that they are not pregnant by signing this consent form.

STORAGE OF BIOLOGICAL TISSUE

If you agree to participate in this study, we will draw up to 5 tablespoons of blood to complete the study visits. Blood may be used for future research to learn more about other diseases. Your samples will be obtained in the Sticht Center at Wake Forest Baptist Medical Center. The samples will be stored at Wake Forest Baptist Medical Center and will be given only to researchers approved by Dr. Suzanne Craft, PhD. All stored biological samples will go to the Alzheimer's Disease Core Center and will be used in future studies as a part of your consent to participate in this study. Samples collected will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive direct benefit from participating in this study. However, your participation may help us better understand brain glucose and ketone body metabolism in adults with mild memory loss and those with pre-diabetes, as well as how brain metabolism may be modified. Study participation may also help us understand how glucose metabolism in other parts of the body may be affected in these individuals. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study.

CONFIDENTIALITY

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. Some of the information we will collect for this research study includes:

- Demographic information
- Vitals including height & weight
- Questionnaires about your everyday activities and feelings
- Social security number (required in order to receive payment)
- Emergency contact information
- Medical record release form (required if we need to request your medical records)

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Suzanne Craft that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Suzanne Craft, PhD
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this consent form you give us permission to use your Protected Health Information for this study.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including study procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $75.00 for each [11C]AcAc/[18F]FDG scan completed up to $150.00 for both scans. If you withdraw for any reason from the study before completion you will be paid for each completed study visit.

Payment schedule – Groups 1, 2 and 3

Participant Payment	**Amount**
Consenting: Visit 1	$ 0
Brain Scan #1: Visit 2	$ 75.00
Brain Scan #2: Visit 3	$ 75.00
Total payment upon study	**$150.00**

To receive payment you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid. Parking will be validated for each visit you attend. No other compensation for study participation will be given.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because unexpected reactions to the study procedures, failing to follow instructions or if the study is stopped early.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by the National Institute of Aging and the Roena B. Kulynych Center for Memory and Cognition Research at Wake Forest School of Medicine.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Suzanne Craft at [redacted] (after hours number [redacted], ask for the Geriatrician on call and reference the AcAc PET study). During this study, Dr. Suzanne Craft and her staff will be monitoring your condition.

The Institutional Review Board (IRB) is a group of people who review research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

The information collected as part of this study will be stored indefinitely for future analyses. We will also collect and store your contact information so that we might offer you the opportunity to participate in future research studies. We will advise you to consult with your physician if your tests suggest that you have a medical problem.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate 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, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institute of Aging which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document including the release of your test results to your primary care physician.

STATEMENT OF CONSENT

By signing this page you are confirming the following:

- You have read all of the information in this consent form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.
- You voluntarily agree to be part of this research study, to follow the study procedures, and to provide necessary information to the study doctor, nurses, or other staff members, as requested.
- You may freely choose to stop being a part of this study at any time.
- You allow the study doctor and the sponsor to use and disclose your personal health information as disclosed in this document.
- You affirm that you are not pregnant.

You will be given a copy of this signed consent form.

You do not give up any legal rights as a research participant by signing this consent form. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.
We can send copies of your test results to your personal physician. Even if you do not wish to have any of your medical information sent to your physician, you can still participate in this research study. Do you request that we send important medical findings from your study tests/exams to your personal physician?

☐ **Yes** ☐ **No** _____ **Subject Initials**

You will be given a copy of this signed consent form.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm

Legally Authorized Representative Name (Print):_____

Relationship to the Subject:_____

Legal Representative Signature: _____ Date:_____ Time:_____ am pm

The above named Legally Authorized Representative has legal authority to act for the research subject based upon (specify health care power of attorney, spouse, parent, etc.)