

ACUC Protocol Recap Sheet

Protocol 449

Title: PET Studies of [¹¹C]AV-45

PI: FOIA (b)
(6) P i

Funding: Avid/Lilly

Others handling animals: FOI A, FOI A, FOIA (b)(6) P i

Animals Approved

Date	Species	Number
03/01/12	Baboons	4

Animals Studied

Date	Species	Number
03/12-01/13	Baboons	1

Approvals

Date	Status	Comments
03/01/12	Initial application	MIRC approval 04/19/12
02/07/13	Continuing review	Effective 03/01/13

FOIA (b)(6) Privacy

From: FOIA (b)(6)
Sent: Tuesday, July 16, 2013 11:03 AM
To: FOIA (b)(6)
Subject: Re: Protocols

That is correct.

From: <FOIA (b)(6) Privacy @bnl.gov>
Date: Tuesday, July 16, 2013 10:19 AM
To: FOIA (b)(6) Privacy @bnl.gov, "FOIA (b)(6) Privacy" <FOIA (b)(6) @stonybrookmedicine.edu>
Subject: Protocols

I understand that there will be no more primate studies conducted here. Currently there are 3 active protocols listing primates. Please confirm this so I can remove training requirements for primate research. Also please inactivate the protocols. Please contact me if you have any questions. Thanks.

FOIA (b)(6)
Privacy


Brookhaven National Laboratory

FOIA (b)

Upton, NY 11973-5000

631 344-FOIA phone

631 344-FOI fax

BROOKHAVEN NATIONAL LABORATORY INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) CONTINUING REVIEW FORM	
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Protocol #:	449
Title:	PET Studies of [11C]AV-45
Principal Investigator:	F [REDACTED] FOIA (b)(6) Privacy
Institution:	BNL
BNL Contact:	

In accordance with BNL Policy, the IACUC reviews all research protocols involving animals no less than annually.
The above protocol is approved until . In order for the IACUC to approve this protocol for another year, please return the completed, signed form and any attachments to FOIA (b) , FOIA (b)(6) by . The period of review is .

1. PROTOCOL STATUS: Please indicate (X) the status of this project by clicking on the appropriate box.	
Request protocol continuance <input type="checkbox"/> Active – project ongoing <input type="checkbox"/> Not started – anticipated start date:	Request protocol termination <input type="checkbox"/> Inactive – project never started x <input checked="" type="checkbox"/> Completed – no further activities will be done

2. RECORD OF ANIMAL USAGE			
Species	Total approved	Used during reporting period	Pain/Distress Category (A, B, C – see below)
Baboons	4	0	

USDA PAIN/DISTRESS CATEGORY LEVEL A: No Pain or Distress: Animals will be euthanized without any treatments or manipulations or irradiation with unrestricted movement and without anesthesia and without anticipated subsequent effects at BNL. LEVEL B: Relieved or Momentary Pain or Distress: Momentary pain or potential pain or distress relieved by pharmacologic, behavioral or other means. e.g., tranquilization/sedation, general or local anesthesia, post-procedural analgesics, behavioral conditioning to restraint or minor pain/stress, medical treatment of disease states LEVEL C: Unrelieved or Sustained Pain or Distress: Any procedure that would cause more than momentary or slight pain or distress. e.g., chronic untreated disease states, pain research

3. LITERATURE SEARCH: For animals used in Level B or C, perform a literature search for alternatives to pain/distress. Please note the Research Library Staff is available to assist with literature searches.

List procedures that may cause pain/distress (e.g. imaging, surgery, injection, behavioral testing, food restriction, etc) and perform a search using the procedures. Procedures that have pain eliminated by the use of anesthetics and/or analgesics are still considered painful even though the animal is not expected to experience any pain/distress.

Date of Search:

Databases Searched:

Years included:

Provide a narrative of Search Results When alternative procedures are discovered, you must identify them and justify why those procedures are not being considered:

4. PERSONNEL

In each box, list all personnel currently working directly with animals and indicate number of years of experience for each procedure for each species.

NAME	SPECIES	MONITORING & HANDLING	NONSURGICAL MANIPULATION	ANESTHESIA, SURGERY	BLOOD COLLECTION	EUTHANASIA

5. PROGRESS REPORT. Please provide a brief but complete, non-scientific description of work done, data collected and conclusions reached, if any, during the past year or a copy of progress reports supplied to DOE, NIH or other funding agency and any publications. If no work has been done, this

should be indicated.

The company terminated the study after this one study.

6. PROBLEMS/ADVERSE EVENTS. Describe any unanticipated adverse events, morbidity or mortality, the cause(s), if known, and how these problems were resolved. If **NONE**, this should be indicated.

None

7. DUPLICATION. Activities involving animals must not unnecessarily duplicate previous experiments. Provide written assurance that the activities of this project remain in compliance with the requirement that there must be no unnecessary duplication.

8. FUTURE PLANS. Please provide a brief non-scientific description of what is to be studied during the coming year (the questions/hypotheses being tested in lay terms). If changes are planned, submit an addendum that outlines planned studies and justification for the proposed changes. *[Please note that if the modifications are significant, you may be required to complete a new application. If you have questions or require assistance in making this determination, please contact the IACUC Office and/or the Attending Veterinarian.]*

none

CERTIFICATION OF THE PRINCIPAL INVESTIGATOR I am aware that all research outlined in this protocol must be carried out under an approved Experimental Safety Review (ESR) and that the protocol must contain the same information as that listed in the approved ESR(s). I am aware that it is my responsibility to ensure that all individuals working on this protocol have been listed on the ESR(s), that their training is appropriate and up to date and that they have read and understood their responsibilities on this protocol.

PRINCIPAL INVESTIGATOR

FOIA (b)(6) Privacy

DATE

7-16-13

Your Department Safety Coordinator will be notified of your IACUC approval.

BNL DEPARTMENT CHAIR

DATE

BROOKHAVEN NATIONAL LABORATORY INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) CONTINUING REVIEW FORM	
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Protocol #:	449
Title:	PET Studies of [¹¹ C]AV-45
Principal Investigator:	FOIA (b) (6)
Institution:	BNL

In accordance with BNL Policy, the IACUC reviews all research protocols involving animals no less than annually.

The above protocol is approved until 02/28/13. In order for the IACUC to approve this protocol for another year, please return the completed, signed form and any attachments to FOIA (b) (6) Pi, FOIA (b)(6) Pi by 01/22/13. The period of review is 03/01/12-01/22/13.

1. PROTOCOL STATUS: Please indicate (X) the status of this project by clicking on the appropriate box.	
Request protocol continuance <input checked="" type="checkbox"/> Active – project ongoing <input type="checkbox"/> Not started – anticipated start date:	Request protocol termination <input type="checkbox"/> Inactive – project never started <input type="checkbox"/> Completed – no further activities will be done

2. RECORD OF ANIMAL USAGE			
Species	Total approved	Used during reporting period	Pain/Distress Category (A, B, C – see below)
Baboons	4	1	B

USDA PAIN/DISTRESS CATEGORY
LEVEL A: No Pain or Distress: Animals will be euthanized without any treatments or manipulations or irradiation with unrestricted movement and without anesthesia and without anticipated subsequent effects at BNL.
LEVEL B: Relieved or Momentary Pain or Distress: Momentary pain or potential pain or distress relieved by pharmacologic, behavioral or other means. e.g., tranquilization/sedation, general or local anesthesia, post-procedural analgesics, behavioral conditioning to restraint or minor pain/stress, medical treatment of disease states
LEVEL C: Unrelieved or Sustained Pain or Distress: Any procedure that would cause more than momentary or slight pain or distress. e.g., chronic untreated disease states, pain research

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List procedures that may cause pain/distress (e.g. imaging, surgery, injection, behavioral testing, food restriction, etc) and perform a search using the procedures. Procedures that have pain eliminated by the use of anesthetics and/or analgesics are still considered painful even though the animal is not expected to experience any pain/distress.

We searched baboon, anesthesia and pain

Date of Search: 1-23-13

Databases Searched: Medline

Years included: 1967-present

Provide a narrative of Search Results When alternative procedures are discovered, you must identify them and justify why those procedures are not being considered:

There were 4 hits. One was relevant and used the same anesthesia that we use.

4. PERSONNEL

In each box, list all personnel currently working directly with animals and indicate number of years of experience for each procedure for each species.

NAME	SPECIES	MONITORING & HANDLING	NONSURGICAL MANIPULATION	ANESTHESIA, SURGERY	BLOOD COLLECTION	EUTHANASIA
FOIA (b)(6) (15 years experience)	baboon	15	15	15	15	NA
FOIA (b)(6) (35 years experience)	baboon	35	35	35	35	NA
FOIA (b)(6) (20 years experience)	baboon	20	20	20	20	NA

5. PROGRESS REPORT. Please provide a brief but complete, non-scientific description of work done, data collected and conclusions reached, if any, during the past year or a copy of progress reports supplied to DOE, NIH or other funding agency and any publications. **If no work has been done, this**

should be indicated.

We did 2 dynamic PET studies with [^{11}C]AV45 in the same baboon on the same day. One covered the brain and the other covered the torso organs. At the end we did a segmented whole body scan to reveal the distribution of C-11 at the end of the study. As predicted brain uptake and clearance were very rapid. C-11 accumulated in the gall bladder and urinary bladder but cleared from other organs.

6. PROBLEMS/ADVERSE EVENTS. Describe any unanticipated adverse events, morbidity or mortality, the cause(s), if known, and how these problems were resolved. **If NONE, this should be indicated.**

none

7. DUPLICATION. Activities involving animals must not unnecessarily duplicate previous experiments. Provide written assurance that the activities of this project remain in compliance with the requirement that there must be no unnecessary duplication.

[^{11}C]AV45 has never been made before and thus this is the first time that its distribution and kinetics have ever been measured.

8. FUTURE PLANS. Please provide a brief non-scientific description of what is to be studied during the coming year (the questions/hypotheses being tested in lay terms). If changes are planned, submit an addendum that outlines planned studies and justification for the proposed changes. *[Please note that if the modifications are significant, you may be required to complete a new application. If you have questions or require assistance in making this determination, please contact the IACUC Office and/or the Attending Veterinarian.]*

The future of this project is uncertain at this time. Though the next stage was to do an IRB application to a comparison with the F-18 labeled version of AV45 in elderly humans, it appears that the company is experiencing budget problems and thus the scope of the project may need to be limited. However, we need to keep this IACUC open until we know for certain.

CERTIFICATION OF THE PRINCIPAL INVESTIGATOR I am aware that all research outlined in this protocol must be carried out under an approved Experimental Safety Review (ESR) and that the protocol must contain the same information as that listed in the approved ESR(s). I am aware that it is my responsibility to ensure that all individuals working on this protocol have been listed on the ESR(s), that their training is appropriate and up to date and that they have read and understood their responsibilities on this protocol.

PRINCIPAL INVESTIGATOR

DATE

Your Department Safety Coordinator will be notified of your IACUC approval.

BNL DEPARTMENT CHAIR

DATE

should be indicated.

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PRINCIPAL INVESTIGATOR

FOIA (b)(6) Privacy

DATE

1/23/13

Your Department Safety Coordinator will be notified of your IACUC approval.

FOIA (b)(6) Privacy

FOIA (b)(6) Privacy

DATE

1/24/13

FOIA (b)(6) Privacy

BROOKHAVEN
NATIONAL LABORATORY

FOIA
P.O. Box 5000
Upton, NY 11973-5000
Phone 631 344-FO
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FOI @bnl.gov

managed by Brookhaven Science Associates
for the U.S. Department of Energy

Memo

* *

DATE: February 13, 2013

TO: FOIA (b)

FOIA
(b)(6)
Privac
v

Digitally signed by FOIA
(b)
Date: 2013.02.13 09:56:54 -05'00'

FROM: FOIA (b)(6), Institutional Animal Care and Use Committee (IACUC)

SUBJECT: IACUC Protocol 449 "PET Studies of [¹¹C]AV-45"

The IACUC approved the continuing review of above the protocol for one year effective 03/01/13 and the new expiration date of this protocol is 02/28/14. This approval is given only for the protocol submitted; any changes must be approved by the IACUC prior to being implemented.

You should be aware that all research outlined in this protocol must be carried out under approved Experimental Safety Review(s) (ESR) and that this application must contain the same information as that listed in the approved ESR(s). You must be aware that it is your responsibility to ensure that all individuals working on this protocol are listed on an appropriate ESR and that their training is up to date.

Please note, other approvals, such as Facility approval, may be necessary.

FOIA
cc: FOIA (b)
FOIA (b)

BROOKHAVEN NATIONAL LABORATORY INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) ANIMAL USE PROTOCOL	 BROOKHAVEN NATIONAL LABORATORY
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The protocol must be submitted in typed form and all applicable items must be answered. Answers must be written in English and in terms understandable to all IACUC members.

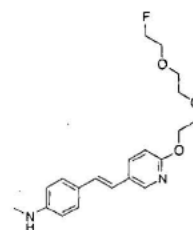
PROTOCOL #:	
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Title	PET Studies of [¹¹ C]AV-45		
Principal Investigator*:	FOIA (b)(6)		
Institution:	BNL		
Address:	Medical Dept, FOIA (b)		
Phone:	631-344-FOIA		
Fax:	631-344-FOIA		
E-mail:	FOIA (b) @bnl.gov		
Key Investigators*:	FOIA (b)(6)		
<small>* Note - if no investigators are BNL employees, please list a BNL employee contact:</small>			
Funding Source: Submit animal methods section of grant	Avid/Lilly	BNL Account Number:	
Protocol Type (e.g. Research, Teaching, Other):	Research/CRADA		
Home Institution IACUC Approval # and dates			

A. OVERVIEW

A.1 Please provide a brief description of the proposed studies in lay terms.

AV-45 is a stilbene derivative which is amenable to labeling with both C-11 and F-18 for plaque imaging. We propose to implement a synthesis method for [¹¹C]AV-45, evaluate biodistribution and dosimetry of [¹¹C]AV-45 in an animal model, and obtain regulatory approval for [¹¹C]AV-45 studies in humans. The long-term goal is to compare these two labeled forms of AV-45 in living humans in order to determine whether their clearance rates differ.



The purpose of this IACUC proposal is to request permission to do PET scans of the brain and the torso area of the baboon after the injection of [¹¹C]AV-45 and to use the organ distribution and kinetics to estimate

radiation dosimetry which is required for an IRB application for evaluation in humans. When the [^{11}C]AV-45 is administered to the baboon it will be given at a tracer dose. We propose to study 4 baboons and each baboon will have 2 injections of [^{11}C]AV-45 administered two hours apart to allow for the decay of the C-11 to background levels.

B. PERSONNEL AND TRAINING

B.1 In each box, list all personnel working directly with animals and indicate number of years of experience for each procedure for each species. All BNL personnel will be put on the appropriate Occupational Medicine Protocol. Non-BNL employees working with primates will be put on the appropriate Occupational Medicine Protocol.

NAME	SPECIES	MONITORING & HANDLING	NONSURGICAL MANIPULATION	ANESTHESIA, SURGERY	BLOOD COLLECTION	EUTHANASIA
FOIA (b)(6)	baboon	14	14	14	14	NA
FOIA (b)(6)	baboon	34	34	34	34	NA
FOIA (b)(6)	baboon	19	19	19	19	NA

Note: Any personnel with less than one year experience in any of the above categories must take the applicable training listed below.

B.2 Indicate which training courses apply to this protocol. Use A to indicate all personnel or put initials of those required to take the training. All courses are located at <http://www.bnl.gov/training>

Required	COURSE TITLE	PROCEDURES COVERED
A	Basic Overview of Laboratory Animal Care and Use	Overview required by all animal users
	Biomethodology of the Mouse	Restraint, handling, identification, sexing, husbandry, behavior of mice
	Biomethodology of the Rat	Restraint, handling, identification, sexing, husbandry, behavior of rats
	Experimental Techniques in Rodents	Injections, blood sampling, oral gavage, euthanasia
	Post-Procedure Care of Mice and Rats: Reducing Pain and Distress	Analgesia, pain & distress recognition and alleviation, post-operative care
	Survival Surgery in Rodents	Anesthesia, aseptic surgical techniques
A	Primate Safety	Covers safe handling of non-human primates
	Controlled Substance Awareness and DEA background Check	Required if any controlled substances will be used
	Regulated Medical Waste Management	Required if regulated medical waste (animal carcasses, needles, syringes) will be generated as a result of the work

C. PROCEDURES

C.1 Concisely describe all manipulations and experimental procedures, including surgeries,

performed on the animals. Everything done to the live animal at BNL must be detailed here. A short description of experimental procedures done elsewhere should be included. Include the end point of the experiment and timing of euthanasia, if applicable. Flow diagrams or charts are helpful. Materials and methods portion of grant applications or other detailed descriptions may be attached.

Anesthesia Procedure (from IACUC 102): Imaging studies require that primates be anesthetized for periods of time not to exceed 8 hours. *It should be noted that all primate studies will be coordinated with other BNL IACUC approved protocols that use these same animals. We make sure that none of these animals is used more frequently than currently approved as a consequence of their being placed on other, BNL approved, IACUC protocols.* **FOIA (b)(6) Privacy** (a nurse and our study coordinator) is responsible for selecting animals for each primate imaging study. She speaks directly with the PI's for the individual study. Scanning the same animal on consecutive days is infrequently required and when it is done, minimal volumes of blood are removed from the animals on the second day. Animals selected for the scanning study are not fed the night prior to scanning, consistent with human studies in which subjects are requested to not eat the night before their scan. None of our human subjects have reported any difficulties complying with this request as a result of pain or discomfort. The morning of the scanning procedure, animals are initially sedated with an intramuscular injection of ketamine hydrochloride (10 mg/kg). Once sedated, the animal is removed from the cage, placed on a clean stainless steel table, covered, and transported to the prep room located just next to the primate unit. Once in the preparation room, the animal is weighed, and a visual inspection of the animal is made prior to beginning the intubation procedure. The animal is then intubated with a laryngoscope and a disposable pediatric endotracheal tube, which is then held in place with Velcro strips. An ambu bag is attached to the endotracheal tube and is compressed in order to determine tube placement and proper inflation of both lungs. Upon verification of tube placement, the cuff is inflated to aid in tube stability. A disposable core temperature probe is then placed into the esophagus for body temperature monitoring. Once this procedure is completed, the animal is placed into a transfer cage and then into the Chemistry Department van. The animal is transported to the PET facility. Upon entering the scanning room, the animal is removed from the transport cage and is placed on the scanning table. The animal's head is then placed into a specific head holder and the endotracheal tube is connected to the anesthesia machine. The gaseous anesthesia used for PET studies consists of isoflurane (Forane® 1.0 - 4.0%), oxygen (1500 ml/min) and nitrous oxide (800 ml/min). Animals are maintained on gas throughout the length of the study. **Gas cylinders (oxygen and nitrous oxide) are checked to assure that they have sufficient gas for an entire study. The regulator pressure on the oxygen tank must be 30 psi.** Prior to arterial and venous line placement, animals are again inspected to ensure that transport didn't change the endotracheal tube or its position. For the duration of the study, isoflurane levels are routinely maintained at between 1.0 – 1.8%. All PET studies require venous and arterial cannulation. For venous cannulations a QuikCath (21 gauge) is placed into a radial arm vein, typically into the antecubital region. Much less frequently, the venous catheter is placed into a vein in the leg located immediately posterior to the gastrocnemius muscle. Regardless of the site, the venous line is maintained with heparized saline under normal pressure. This venous line is used for radioisotope and pharmacologic drug injections only.

In order to evaluate PET data, arterial blood is drawn from the animal throughout the duration of the study. Arterial cannulation is performed using a QuikCath (21 gauge) most typically along the mesial aspect of the popliteal region of the leg. Much less frequently, arterial cannulation occurs in the lower aspect of the inguinal region. On rare occasions, radial or ulnar arterial cannulation is performed. Upon establishing the arterial line, a blood sample is drawn for hematocrit determination. The arterial line is maintained with heparinized saline under pressure to slightly exceed normal resting states. The arterial line is then connected to a pediatric pressure transducer for invasive monitoring of heart rate and blood pressure using a SpaceLabs Pediatric Patient Care Monitoring System. During the study, blood is drawn continuously for the first 2 minutes and then at selected times throughout the scanning period. For all baboons used under this application, any given radioisotope injection includes no more than 100 mls of

blood sampling. Immediately following arterial cannulation and blood pressure monitoring, chest leads are connected for electrocardiogram (EKG) monitoring, the temperature probe is connected for core temperature monitoring, a respirator monitor is connected for respiration monitoring, and finally, the system is set to alarm should any vitals fall outside a well delineated range specific for each animal. Upon completion of these procedures, a disposable blanket is placed over the animal and connected to an electric heating unit that maintains warm air circulation in order to keep the animals' core temperature to within a specific range. Once this animal preparation is completed, usually within 30 minutes, the animal is placed into the tomograph for the necessary preliminary scans to be completed prior to radioisotope injection. Radioisotopes and specific drugs detailed in this proposal are injected via an intravenous line. Specifically, drugs used in all studies are injected at pre-selected intervals (pretreatment times) in order to maximize the CNS effects. Drugs are typically administered as a bolus but in certain cases, drugs may be administered over a period of minutes to hours as drug safety dictates. Drugs are also sometimes administered via nasogastric tube which is installed after the animal is anesthetized. The nasogastric tube placement is always checked prior to administration of any fluid or drug. This is to prevent aspiration if the tube placement was wrong.

Commencing with radioisotope injection, an automated blood sampling machine (Ole Dich) is activated and blood (For all non-human primates used under this application, any given radioisotope injection includes no more than 100 ml of blood sampling.) is continuously drawn for the first 2 minutes. Blood samples are placed into pre-heparinized vials for further analysis. This sampling interval removes approximately 17 ml (for all non-human primates used under this application) over 2 minutes. During the entire scanning procedure, vital signs are automatically recorded and strips of the EKG trace are printed and placed into the experimental records. At the end of the scanning procedure, the venous line is removed and held off for at least 5 minutes. The arterial line is then removed and pressure is continuously applied for at least 10 minutes, with observations made after 5 mins. Once the line has been determined to be closed, the animal is removed from the anesthesia machine. At this point, only oxygen is administered, i.e., both isoflurane and nitrous oxide are shut off. Ketamine is available should the animal require additional sedation during transport. The use of ketamine following a study for this purpose is extremely rare. Generally, within 15-20 minutes the animal has a positive eye-lid response and begins to cough. The endotracheal tube is removed and the animal is placed back into the cage, now containing an absorbable and disposable diaper, and is transported back to the BLAF. Once back in her home cage, the animal is frequently checked and must be able to sit up on her own before the last team member leaves for the day.

For this study we will scan 4 baboons with [^{11}C]AV-45. Each baboon will be anesthetized, have an arterial catheter placed and be scanned twice, 2 hours apart with the brain and peripheral organs in the field of view. Scans will last for 60 minutes. Arterial blood will be taken over the time course of the study. Depending on the size of the baboon more than one scan position may be required over the torso in order to cover all of the organs. Thus for two of the baboons, there will be one brain and one torso scan and for the other two there will be two torso scans one covering the upper torso and the other covering the lower torso.

C.2 Does this work duplicate previous experiments/activities? If yes, justify.

no

D. ANIMAL DESCRIPTION

D.1 Species:	Baboon
D.2 Strain/Breed:	Papio anubis
D.3 Sex:	female
D.4 Age/Weight:	Young adults – 30 years
D.5 Supplier:	BNL

*If not a commercial vendor, a recent health report (no older than three months) from the animal facility must be submitted to the BLAF Manager **at least six weeks before** the planned experiment or shipment of animals. Please contact the BLAF Manager at 631 344-FOIA (b)(6) to make arrangements for the receipt of the animals.*

D.6 Justify that the work is appropriate to be done in an animal model.

The baboon is used as a model for the human in order to obtain the best estimate of the distribution and clearance rates of the radioactivity which will serve as the best possible input for radiation dosimetry estimations.

D.7 Justify species to be used and why a lower phylogenetic species cannot be used.

We use primates primarily because the physical size of their brains and peripheral organs in combination with the known resolution of the PET camera is the optimal model for estimating the radiation dosimetry which would be expected in humans. The baboon model also allows us to obtain an arterial input function which is also useful in our dosimetry estimation and in our research.

D.8 Animal Numbers	
D.8.a Total for first three years:	N=4
D.8.b Maximum housed at one time:	N=4

D.9 Justify number of animals. Indicate design of study groups and statistical methods and include power calculations. Include steps taken to minimize the number of animals required.

This is an observational study. We chose 4 animals in order to do repeated measures in the brain and repeated measures in peripheral organs and to obtain complete coverage of the peripheral organs which is not always possible in one scan over the torso.

E. PAIN/DISTRESS
E.1 List total number of animals at applicable levels of stress/discomfort

<p>Level A: No pain or distress: Animals will be euthanized without any treatments or manipulations or irradiation with unrestricted movement and without anesthesia and without anticipated subsequent effects at BNL.</p> <p>Level B: Relieved or momentary pain or distress: Momentary pain or potential pain or distress relieved by pharmacologic, behavioral or other means, e.g., injection of any substance including anesthetics, post-procedural analgesics, behavioral conditioning, restraint or minor pain/distress and medical treatment of</p>

disease states.

Level C: Unrelieved or sustained pain or distress: Any procedure that would cause more than momentary or slight pain or distress, e.g., chronic untreated disease states, pain research

Species	LEVEL A	LEVEL B	LEVEL C
baboon		4	

E.2 For animals used in Level B or C, perform a literature search for alternatives to pain/distress.

Please note the Research Library Staff is available to assist with literature searches.

List procedures that may cause pain/distress (e.g. imaging, surgery, injection, behavioral testing, food restriction, etc) and perform a search using the procedures. *Procedures that have pain eliminated by the use of anesthetics and/or analgesics are still considered painful even though the animal is not expected to experience any pain/distress.*

I searched baboon, anesthesia and pain on 2-12-12

Date of Search: 2-12-12

Databases Searched: Medline

Years included: 1967-present

Provide a narrative of Search Results *When alternative procedures are discovered, you must identify them and justify why those procedures are not being considered:*

I got 4 hits, two of which were relevant. These two used the same anesthesia (ketamine then isoflurane) that we are currently using.

E.3 Indicate how procedures have been refined to reduce the amount of potential pain, distress or morbidity.

We allow at least 4 weeks for recovery after each baboon PET session. We optimize the information from each scan session scanning 2-3 times for one anesthesia, blood sampling session. When appropriate to the study goals, we always use the animal as her own control in test-retest protocols which reduces the need to consider inter subject variability thereby reducing animal numbers.

E.4 Describe if animals are subjected to food/water deprivation or prolonged and/or unusual restraint and provide justification. *Describe how animal health is monitored during deprivation.*

Animals are fasted overnight which is routine procedure prior to anesthesia

E.5 Is death used as a study endpoint wherein animals must die without intervention such as pain relief and/or euthanasia? *If yes, explain why an earlier end point is not acceptable.*

no

F. ANIMAL CARE

F.1 Please indicate if animals will be housed (kept for more than 24 hours) at BNL in other than in the Brookhaven Laboratory Animal Facility (BLAF).

Not applicable

F.2 Describe additional requirements for other than routine animal care (e.g. housing, feeding, hazardous waste bedding disposal) *Investigative staff must be responsible for feeding all animals, weighing the correct amount of food, logging each feeding and adjusting the ration as needed to maintain the animal at the desired weight. If food, equipment and/or other supplies are to be shipped from another institution's animal facility, a recent health report from the facility must be submitted to the BLAF Manager at least six weeks before the planned experiment.*

All care is routine except when PET staff stay with a baboon in BLAF until she recovers from anesthesia after a PET study.

F.3 Scientifically justify if singly-housed rodents will not be provided with environmental enrichment.

Not applicable

F.4 List the building and room number(s) in which experimental procedures, surgery, and/or postoperative recovery will be performed on live animals (if known).

Initial knockdown and intubation of the baboons is done at BLAF. Arterial catheterization and anesthesia induction and maintenance and radiotracer injection and blood sampling is done in either PET rooms 5 or 6 in bldg 906. Baboons recover from anesthesia in their home cage at BLAF.

G. PROCEDURE SPECIFICS

G.1 List all chemical agents (sedatives, analgesics, anesthetics, paralytics, euthanasia, study drugs, radiotracers) administered to the animals. *For euthanasia involving CO₂, please use 100% CO₂ at a 20% air replacement per minute rate. For ketamine anesthesia, please use intraperitoneal (ip) injections, not intramuscular (im). Ketamine/xylazine may be stored for up to 28 days after mixture.*

Type	Agent	Dose	Route	Frequency	Controlled Substance (Y/N)
------	-------	------	-------	-----------	----------------------------

anesthesia	ketamine	10 mg/kg	im	Initial knockdown and as needed	Y
anesthesia	Isoflurane	Forane [®] 1.0 - 4.0%	inhalation	As needed	N
Radiotracer	AV-45	2 mCi	IV	Twice	N

G.1.a List the name(s) of the individual(s) administering the above agents:

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G.1.b Indicate building and room numbers where agents are stored and security procedures for controlled substance(s):

All controlled substances are kept in double-lock boxes in the HOT Laboratory in 901 or in the exam room in 906 or the microPET lab in 906.

G.1.c If paralytic agents are used in conjunction with surgical manipulations, indicate the means by which absence of pain is monitored and/or determined, and who is responsible:

Not applicable

G.2 Is surgery involved? *If yes, indicate whether surgery is survival or non-survival.*

no

G.2.a Describe monitoring and supportive care provided during surgery (who, what and how will this be done?):

Not applicable

G.2.b Describe indications for analgesic therapy to be administered before, during, and/or following surgery:

Not applicable

G.2.c Describe post-operative and/or anesthetic monitoring and supportive care (who, what and how often): Please use Surgery and Recovery Record

Also see primate procedure. Once back in her home cage, the animal is frequently checked and must be able to sit up on her own before the last team member leaves for the day.

G.2.d Who will maintain surgical and post-operative records and where will they be maintained? Please note: Records must be accessible for inspection

FOIA (b)(6) and FOIA (b)(6) maintain these records in the drawer of the cart in room 6 of Bldg 906 (PET Lab).

G.3 Is anesthesia involved?

yes

G.3.a Describe monitoring and supportive care provided during anesthesia (who, what, and how

will this be done?): **Please use Surgery and Recovery Record**

See C1

G.3.b Who will maintain anesthetic records and where will they maintained? Please note: Records must be accessible for inspection

FOIA (b)(6) and FOIA (b)(6) maintain these records in the drawer of the cart in room 6 of Bldg 906 (PET Lab).

G.4 Are animals to be used in more than one major surgical procedure from which they are allowed to recover? If yes, please describe and justify.

no

G.5 By what method and by whom will animals be euthanized and how will death be confirmed? If a chemical agent is used, please list in Section G.1. For euthanasia involving CO₂, please use 100% CO₂ at a 20% air replacement per minute rate. Justification must be provided for any physical method, such as decapitation or cervical dislocation, without anesthesia.

Not applicable

G.6 List criteria for intervention and/or removal of animals from study or early euthanasia.

• Examples are severe ataxia; rapidly increased heartrate or respiratory rates; oral, nasal or vaginal discharge such as pus or blood; wound dehiscence; marked swelling, tumor(s) greater than 2 cm or ulcerating, ulcer greater than 10% of body surface area, inability to eat or drink, loss of weight, great discoloration in an appendage or surgical area; immobility.

• Unless otherwise noted 100% CO₂ at a 20% air replacement per minute rate will be used for early euthanasia for rodents.

Baboons will be removed from the PET study early if their vital signs show indications of distress.

H. SPECIAL CONSIDERATIONS

H.1 Check materials that are hazardous to personnel being used in this study.

<input type="checkbox"/> Human cells or fluid	<input type="checkbox"/> Microorganism	<input type="checkbox"/> Chemicals including fixatives	<input type="checkbox"/> Recombinant DNA
<input type="checkbox"/> Nanoparticles	<input checked="" type="checkbox"/> Radioactivity (isotopes)	<input type="checkbox"/> Other (list)	<input type="checkbox"/> Irradiation

For each agent listed above, please ensure that it is covered under an approved ESR

H.2 Indicate if animals will be shipped from BNL. If yes, indicate that BNL's preferred shipping procedures will be followed. If other arrangements are necessary, please describe.

Not applicable

I. INVESTIGATOR ASSURANCE

I affirm to the best of my knowledge that all the above information is complete and accurate and agree to accept responsibility for this project in accordance with applicable Federal and State of New York regulations, USDA guidelines, and established BLAF policies and procedures. No changes will be made without prior approval from the IACUC.

In order to reduce risk to all personnel and laboratory animals, I agree to:

- Follow BNL procedures for aspects of the animal care and use such as preoperative care, anesthesia, surgical technique, postoperative care, sampling techniques, euthanasia, and disposal of contaminated carcasses and waste.
- Ensure that my instructions to laboratory personnel are implemented.
- Ensure that all project personnel comply with the required Occupational Health Program before handling animals.
- Instruct all personnel in my laboratory that they should inform me if they believe that the treatment of any research animal is inappropriate. If the situation is not resolved, the employee should contact the Attending Veterinarian, or the IACUC Chair and/or Institutional Official.

I am aware that all research outlined under this protocol must be carried out under approved Experimental Safety Review(s) (ESR). I am aware that it is my responsibility to ensure that all individuals working on this protocol have been listed on an appropriate ESR and that their training is up to date. I am aware that work cannot proceed without an approved ESR.

PRINCIPAL INVESTIGATOR	FOIA (b)(6) Privacy	DATE	2/15/2012
Your Department Safety Coordinator will be notified of your IACUC approval.			

J. APPROVALS

I attest that the following issues have been appropriately addressed: Scientific merit of project; Appropriateness of conducting the project at BNL; Adequacy of funding for the project; Appropriateness of the expertise and experience of the PI and project personnel; Appropriateness of training for the PI and project personnel, and; Adequacy of department resources to support this protocol.

FOIA (b)(6) Privacy	FOIA (b)(6) Privacy	DATE	2/29/12
PHARMACIST (or designee)		DATE	
Required for Schedule I controlled substances			

FOIA (b)(6) Privacy

From: FOIA (b)(6)
Sent: Wednesday, January 23, 2013 8:33 AM
To: FOIA (b)(6)
Subject: FW: IACUC Protocol 449
Attachments: Form005status.memo.doc

Reminder: This form is due. Thanks.

FOIA

From: FOIA (b)(6)
Sent: Friday, January 04, 2013 2:56 PM
To: F
Subject: IACUC Protocol 449

Attached please find the Continuing Review form for the above protocol. Please e-mail the completed form to me by 01/22/13 and fax the signature page to 631 344- for send as a pdf. Please answer all questions even if no work has been performed during the past year. Annual literature searches for alternatives are required for all protocols involving animals in pain/distress Category B and/or C.

FOIA (b)(6)

Privacy

Brookhaven National Laboratory

FOIA (b)

Upton, NY 11973-5000

631 344-FOI phone

631 344-FOI fax

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F FOIA (b)(6)
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