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Document:
Consent To Participate In Research

Study Title:
Imaging [^{18}F]PI-2620 and Florbetaben F18 in military service members with blast-related mild traumatic brain injury

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National Intrepid Center of Excellence (NICoE), Walter Reed National Military Medical Center (WRNMMC)

CONSENT TO PARTICIPATE IN RESEARCH

Title: Imaging [^{18}F]PI-2620 and Florbetaben F18 in military service members with blast-related mild traumatic brain injury

Principal Investigator: Grant H. Bonavia, MD, PhD

You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to carefully review this information. You should talk to the research team about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal doctor) about your potential participation in this research study. You do not have to take part in this study. Participation is voluntary. You may also leave the research study at any time without penalization.

1. KEY INFORMATION:

Participation in this research study is voluntary. The study uses neuroimaging (brain imaging) and neuropsychological testing to look at potential changes in brain structure and function in members of the military who have a history of blast-related mild traumatic brain injury (mTBI) compared to two control groups. The study takes place over two visits and requires up to a total of 13 hours over two days. Participants will undergo two positron emission tomography (PET) scans, 2 computed tomography (CT) scans (as part of the PET scans), one magnetic resonance imaging (MRI) scan and neuropsychological testing. Participants will also be asked to answer questionnaires as well as choose a study partner who will answer questions about the participant. Risks and discomforts may include exposure to small amounts of radiation, a small chance of mild and quick- resolving side effects from the radioactive agents or tracers used in the PET scans and needle stick, discomfort in the MRI scan such as claustrophobia, and feeling uncomfortable or tired during the neuropsychological testing and questionnaires. One of the radiotracers used in this study ([^{18}F]PI-2620) has been used in only 3 prior studies. These and other potential risks are described in detail below. This study may benefit other members of the military in the future who are experiencing behavioral and cognitive complaints which may be related to brain changes from blast exposure and mTBI. The alternative to participation in this study is to not participate.

Your decision will not affect your future care at Walter Reed National Military Medical Center (WRNMMC) or the National Intrepid Center of Excellence (NICoE). If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand all sections of the consent form, including the risks and possible benefits to you.

Please tell the research team if you are taking part in another research study.

2. WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?

You are being asked to take part in this research study because you are either a Defense Enrollment Eligibility Reporting System (DEERS)-eligible (eligible to receive military benefits such as TRICARE) service member or an active duty service member currently or formerly enrolled in NICoE's Intensive Outpatient Program (IOP), you are 54 years old or younger, you either have not or have been exposed to blast during a deployment, have had an mTBI or have had no history of TBI, and you may not or may have blast-related mTBIs resulting in problems with thinking and memory. An mTBI effects the normal function of the brain. The purpose of this research study is to develop a way to identify brain regions affected by mTBI using brain imaging and learn about how exposure to blast and head injury are related to changes in cognition (ability to think) and brain structure. Research has shown that exposure to blast and head injury can lead to cognitive problems later on in life and may be connected to the development of disorders such as Alzheimer's disease and what has been called chronic traumatic encephalopathy (CTE). New brain imaging technology could help us learn what role different types of head injury play. We are using this imaging to investigate areas of the brain that might be damaged or functioning differently, and if brain scans can be used to diagnose a pattern of damage specific to either Alzheimer's disease or CTE. During the study, you will have 2 visits which will take place over 2 days at NICoE and will be scheduled back-to-back when possible. The duration of participation per day is between 4 to 6.5 hours. The first day will take about 6.5 hours, which includes time for lunch after scanning or breaks as needed during testing, and the second day will take about 4 hours with time for breaks. The study time may be shorter if you have already completed some of the same tests at NICoE as part of your care in the IOP.

There will be approximately 30 people taking part in the study at NICoE over a period of 1 year.

We are evaluating an investigational radiotracer drug [^{18}F]PI-2620 (a diagnostic agent) in this study. This radioactive agent detects clumps of a substance or protein called tau in the brain. Tau protein is a naturally occurring protein in the brain. Accumulation of tau proteins in the brain form structures called neurofibrillary tangles. These tangles are associated with Alzheimer's disease and CTE.

The Investigational New Drug (IND) [^{18}F]PI-2620 has not yet been approved for routine clinical use by the Food and Drug Administration (FDA). The FDA has authorized an IND for this research study. Previous studies on this diagnostic drug (radiotracer) have demonstrated safety and efficacy; this investigational diagnostic radiotracer has been identified as a promising compound for tau PET imaging. No serious adverse events have been reported during use, according to the investigator brochure. However, it has not yet met the rigorous safety and efficacy criteria necessary for full FDA approval.

As this is a research study, the clinical and research results will not be shared with you.

3. SCREENING PROCESS TO QUALIFY FOR PARTICIPATION IN THIS STUDY

Before you can take part in this study, you will need to have some tests and provide some information so that the investigators can confirm that you qualify for the study. This is called the "Screening Process". These tests may have been previously performed or this information collected as a part of your regular medical care.

You will have already had a screening interview to identify any diagnoses or symptoms you may have and confirm eligibility. Additionally, staff may access medical information to confirm eligibility. Prior to completing the scans, the neuroimaging technicians will ask you questions to make sure the scans are safe for you to complete, such as if you have any metal in your body.

Some of the information gathered during screening may be used for the research study if you decide to participate. If you choose not to participate or are ineligible, the data gathered will be destroyed. The results of a physical examination or medical and psychiatric history that may have been obtained during your standard clinical care at NICoE may also be used in this study. If the screening procedures confirm you are eligible to participate in this study, a time will be scheduled for you to come to NICoE to complete the study procedures.

4. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

You will be asked to come to NICoE to complete the study procedures over 2 days. The day 1 visit will take about 6.5 hours or less (including time for lunch and/or breaks) and the day 2 visit will take about 4 hours (with time for breaks). All procedures will take place in the NICoE Research Department.

Study Procedures:

Neuropsychological Assessment and Questionnaires:

The neuropsychological assessment is a group of pencil and paper tests that measure your memory and thinking abilities. In total it takes about 4 hours to complete and this will take place on Day 1 or 2 depending on availability. The questionnaires ask about things like your moods, activities, and functioning. If you have already received a neuropsychological assessment and completed questionnaires as part of your care at NICoE within the past 4 weeks, the previously completed assessments will be used for this research and you will not be tested again on the same measures. There are some additional questionnaires for the study that you will need to complete. If you have not had the testing done or if you need to complete the additional questionnaires, you will complete the testing and questionnaires on the day of your first or second visit.

We will also ask you to name a study partner (a spouse, partner, adult child or close friend that has known you and maintained close contact with you for at least 2 years). The study partner does not have to attend the study visit with you, but must be available to answer some questions over the phone about your health and daily functioning. We will not disclose any study results or personal information to your study partner.

The study partner will complete the following three questionnaires in reference to the research participant, which will be used to corroborate behavioral and cognitive problems and history of brain injury:

○ Neuropsychiatric Inventory Questionnaire (NPI-Q): Measures neuropsychological symptoms
○ Clinical Dementia Rating (CDR): Characterized domains related to dementia
○ Functional Activities Questionnaire (FAQ): Measures activities of daily living

The questionnaires will not change based on the participant's health status.

Florbetaben F18 (amyloid) PET Scan:
You will have a PET scan using a radioactive tracer called Florbetaben F18. Florbetaben F18 has been approved by the FDA for use in PET imaging. It binds to a substance (protein) called beta-amyloid which is a sticky protein that gathers into structures called plaques in the brain of people who suffer from Alzheimer's disease. For this PET scan, an intravenous line (IV) will be inserted into a vein in one arm for the injection of the Florbetaben F18 radiotracer. After you are injected with the radioactive tracer, you will be asked to rest quietly in a room for 90 minutes to allow it to circulate. The scan will begin after 90 minutes.

The PET scanner is a large, donut-shaped computer-assisted device. You will lie on a narrow bed with your head inside the donut hole, where the scanner will take pictures of your brain. Your head will be stabilized by a soft strap and it will be necessary for you to lie in place without moving while the scanning process takes place. The duration of the PET scan is approximately 20 minutes.

[^{18}F]PI-2620 (tau) PET Scan:
You will complete a second PET scan using a tracer called [^{18}F]PI- 2620. This radiotracer is being studied by the FDA as a diagnostic tool for different types of dementia. [^{18}F]PI-2620 is not currently approved for routine clinical use by the FDA. The research sponsor intends to apply for FDA approval with support from data collected in this study as well as other research studies conducted on [^{18}F]PI-2620. This tracer binds to a substance (protein) called tau. The tau protein gathers inside brain cells and forms structures called "neurofibrillary tangles". These tangles are associated with both Alzheimer's disease and CTE.

This PET scan involves a very similar procedure to the Florbetaben F18 PET scan you will have had the day before. Like the Florbetaben F18 scan, an IV will be inserted into a vein in one arm for the injection of the tracer. You will be placed in the in the same machine that you had the Florbetaben F18 PET scan. Once you are injected with the tracer you will be placed in the scanner and scans will be acquired for 0 to 60 minutes post injection. It will be necessary for you to lie in place without moving while the scanning process takes place.

MRI Scan:
In addition to the PET scan, you will have a structural brain scan called an MRI. If you have consented to an MRI scan as part of the Core Imaging Protocol at NICoE, we will ask your permission to use that scan for this study; other data will not be shared between these studies, only the scan. If you do not give permission, the scan will be repeated. If you previously were enrolled in the IOP program

and received an MRI you may need to repeat the scan for accuracy. MRI involves taking pictures of the structure of your brain using a powerful magnetic field as well as radio waves, much like the kind that transmit music on the radio. The combination of radio waves and the magnetic field allows for the production of very clear images of the brain. You will hear loud "clicking" and "banging" sound during the procedure, which are a normal part of the process. As with taking regular pictures with a camera, if you move, the pictures will be blurred and unusable. You must remain very still while you are inside the machine being scanned. In total, you will be inside of the MRI scanner for about 90 minutes. No contrast agent will be used for the MRI scan.

Please initial the sentence that reflects your choice:

____I do not authorize the use of a previously collected MRI scan to be shared and used for this study.

____I authorize the use of a previously collected MRI scan to be shared and used for this study.

____This is not applicable to me.

The MRI scans will be read by a neuroradiologist who is a doctor that specializes in the use of x-rays and other scanning devices for the diagnosis of disorders of the nervous system. PET scans will be read by a nuclear radiologist who is a doctor that specializes in radioactive substances.

A member of the study team will contact you approximately 30 days after your last visit to check in and ask if you had any unreported side effects. We may contact you if we need further information or if your scans might show clinical signs which warrant discussion.

All of the procedures in this study will be done solely for research purposes. It is important for your safety and for the scientific portion of the study that the investigators are fully informed about any past medical or psychiatric conditions you may have now or have had in the past.

If you have had a PET scan during the past year, you must tell the investigators. Also, you must agree to tell them about any past or present exposure to any drugs (including alcohol and tobacco) such as sleeping pills, marijuana, amphetamines, "recreational drugs" which affect the brain, or if you have been exposed to radiation or X-rays. You will not be allowed to participate if you are currently using any of these drugs or have had more than two PET scans during the year, which exposed you to radiation. You must also inform the investigators of any history of epilepsy, head injury, liver, untreated thyroid, bladder or kidney disease, and any allergies.

You may not continue in the study if you have any metal implants or any ferrous (metal) materials in your body that would interfere with the MRI scan; some metals such as titanium may be safe for the MRI, but you must disclose all metals to the study staff so they may make an appropriate safety assessment. Also, the investigator can discontinue you from the study if you do not follow procedures or show up for your appointments.

5. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

If you choose to take part in this study, there is a risk of:

Risks from the Florbetaben F18 and [^{18}F]PI-2620 PET scans:

As a result of participating in this study you will be exposed to some radiation from the PET scans of your brain. The following information will help you understand how much radiation, and the risks from the radiation.

Radiation is measured in units called "millisieverts" (mSv). A PET scan exposes you to about 9 mSv of radiation. A single chest x-ray exposes the patient to about 0.1 mSv. This is about the same amount of radiation people are exposed to naturally over the course of about 10 days. We are all exposed to radiation on a daily basis from natural sources such as the sun, or artificial sources such ascomputer screens and cell phones. The average yearly exposure for people living in the USA from these sources is approximately 6.2 mSv a year. The United States Nuclear Regulatory Commission (NRC) recommends limits for additional radiation exposure per year. For the General Public, the recommended yearly additional exposure limit is 1 mSv. For people who work with radiation, such as X-ray technicians, the recommended yearly exposure limit is 50 mSv.

In this study you will be exposed to a total of about 12.3 mSv of radiation from both PET scans (5.8 mSv from the Florbetaben F18 PET scan, 6.1 mSv from the [^{18}F]PI-2620 PET scan and an additional 0.4 mSv from the CT portion of both PET scans). This is more than the average annual exposure (6.2 mSv) and more than the NRC recommended yearly limit for the general public (1 mSv) but less than the yearly limit for those who work with radiation (50 mSv).

The study doctors will always try to limit radiation exposure, and will discuss the radiation involved in this study with you. The radiation exposure from this study will be in addition to any exposure you may get from other tests or treatments you may have that involve radiation. If you are going to have any of these, please let the study team know.

Additionally, [^{18}F]PI-2620 is being tested as a tool for identifying tau pathology in people with Alzheimer's disease and other neurodegenerative diseases. Tau pathology is defined as the abnormal accumulation of tau proteins in the brain. Preliminary safety studies have shown a small number of negative effects such as elevated blood pressure, hypokalemia (low blood potassium levels), pain in the upper extremity, flushing, diaphoresis (excessive sweating), and exacerbation of rosacea. These effects were considered mild in severity and resolved with symptomatic intervention, meaning adverse events that participants experienced were resolved with the appropriate treatment for each ailment. This information was directly sourced from the Investigational New Drug (IND) brochure for [^{18}F]PI-2620. The specifics of individual treatments were not provided in the brochure. Other negative effects included numbness in the upper extremity, anxiety, dizziness, diarrhea, injection site reactions consisting of erythema (superficial reddening of the skin), irritation and pain. These were also considered mild in severity and resolved without any intervention.

The FDA approved package insert describes the risk of negative events related to Florbetaben F18

injection. Safety data is based on data from studies from 1090 administrations of Florbetaben F18 to 872 subjects. No serious adverse reactions related to Florbetaben F18 administration have been reported. The most frequently observed adverse drug reactions in subjects receiving Florbetaben F18 were injection site reactions consisting of erythema (skin redness) (1.7%), irritation (1.1%), and pain (3.4%). All negative reactions were mild to moderate in severity and of short duration.
This information was sourced from page 1 of the Florbetaben package insert under the header "Adverse Reactions" as well as Section 6.1.

You may have a bruise or be sore at the site where the radiotracer is injected from the needle. There is also a slight possibility of infection at the injection site. This is unlikely and carries the same risk as any routine needle stick. All needle and IV placements will be performed by a trained technician using a sterile needle. PET radiotracer injection will also be performed by a trained technician.

Risks from Magnetic Resonance Imaging (MRI):
Some people have a claustrophobic reaction to small spaces while in the MRI scanners. Further, some people find the amount of noise produced by the MRI uncomfortable. For this reason, earplugs may be provided. If you have any surgical clips or metallic prostheses (such as artificial hip or knee, shrapnel, or other metal implants), you may not be able to participate in this study. No short-term risks have been reported for MRI; longer-term risks are under evaluation.

Some people may have a claustrophobic reaction, which means that they feel scared of being enclosed in a small space, while in the MRI or PET scanner. It is important to realize that the scanner is open at both ends, and technicians are constantly in communication with you via a microphone system. If you feel anxious or scared inside the machine, our research coordinator, who will be sitting outside with the operator during the scan, will offer you support. It helps some people to wear an eye mask during the MRI scan which can be provided if you would like to wear one. If you continue to feel claustrophobic, you can ask to stop the scan.

If the MRI scan report demonstrates a clinically significant finding, the Principal Investigator will inform you so you can seek out further care. The results from the tau and amyloid PET scans will not be disclosed to participants as they are experimental.

If incidental findings are discovered on any of your scans, they will be documented in your medical record, reported to your medical provider(s), and may impact your ability to serve in the military

Risks from Neuropsychological Assessment and Questionnaires:
Some of the questions asked may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and go to the next question. During the neuropsychological testing, you may begin to feel tired. If this is the case, you can ask the staff member giving the test to take a break until you feel ready to continue with testing. You may also feel embarrassed about testing performance. If results from the testing warrant clinical follow-up, you may be contacted.

Although efforts are made to protect your research study records, there is always a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.

For those on active duty, we may be required to report illegal activities to your Commanding Officer,

such as drug use, which may affect your military career.

Please **Initial** to confirm you have read the above statement. _____

There may also be other risks of taking part in this study that we do not yet know about.

6. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?

There are no direct benefits to you for taking part in the study. However, others may benefit in the future from the information learned during this study. The possible benefits to others are that the study will inform investigators about brain function in memory and behavior disorders and how a history of head injury or mTBI can contribute to these problems.

Potential additional clinical information gleaned from the MRI scan could be a potential benefit for participants, when applicable.

7. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

Your alternative is not to participate in this research. You may decide not to participate without any penalty. Any treatment you are receiving as part of your care by your doctors, NICoE, WRNMMC, or any other institution will not be affected by your participation in this study. This study is not designed to provide treatment. The MRI and neuropsychological testing are available clinically, not as part of the research. Also, the research team may contact you following your participation to collect any missing information. In addition, the research team would like to contact you at a later time about participating in future studies.

8. IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?

Non-active duty/non-federal employee or active duty/federal employee on leave with command approval may receive maximum compensation of $300, based on the study assessments completed. Active duty members who are on-duty are not eligible to be paid for participation.

In order to compensate you for the trial, we will ask you to complete a W-9 form on the first day of your study visit if you are receiving a single payment of $75 or multiple payments totaling $150 or more in a calendar year. The W-9 will include your Social Security Number (SSN). This form will be sent to the Henry M. Jackson Foundation (HJF) through a secure file server for their records. If you make more than a total of $600 per calendar year by participating in research studies conducted through HJF, then you will receive a Form 1099. Your compensation in this study will be made to you through a reloadable debit card through HJF and their business associate Greenphire. Your information is protected through limited access and the information is password protected.

9. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study. The testing and scans are done free of charge. However, you may have costs associated with your participation including travel to and from NICoE, childcare costs, or time off work. You will not be reimbursed for these costs.

10. PRINCIPAL INVESTIGATOR (the person(s) responsible for the scientific and technical direction of the study):

Principal Investigator: Dr. Grant H. Bonavia, MD, PhD Phone: 301-319-3713
Mailing Address: National Intrepid Center of Excellence Walter Reed National Military Medical Center, 4860 South Palmer Road, Bethesda, MD 20889

11. STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):

Life Molecular Imaging (LMI) is the sponsor of this study. The Center for Neuroscience and Regenerative Medicine (CNRM) at USUHS funded this study and will also assist in data analysis.

As the sponsor of this research, the Department of Defense may have access to your research data in accordance with DoDI 3216.02.

12. SOURCE OF FUNDING:

This study is funded by CNRM. The CNRM was created as a research partnership between military treatment facilities in the National Capital Area and the National Institutes of Health (NIH). The CNRM focuses on the diagnosis and treatment of traumatic brain injury (TBI).

13. LOCATION OF THE RESEARCH:

Your study participation and the study activities will take place in the research wing of NICoE which is located on the WRNMMC campus.

14. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

No members of the research team have any financial conflicts of interest with the sponsor of the study or the supplier of the radiotracers used in the study. The Florbetaben F18 and [^{18}F]PI-2620 ligands are being supplied by Life Molecular Imaging. The company manufacturing and providing these ligands have a financial interest that could be affected by the outcome of this study.

15. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at:http://www.dtic.mil/whs/directives/infomgt/forms/eforms/dd2005.pdf

The research team will keep your research records. These records may be looked at by staff from the NICoE, CNRM, the Institutional Review Board (IRB), and the DoD Higher Level Review as part of their duties. These duties include making sure that the research participants are protected. LMI will also view your PET and MRI images to assist with quantitative assessment of scans. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to:

- Data will be coded: you will be given a unique study ID number that will be used throughout the study. Only designated study staff will have access to link between the ID and your name; the link will be kept in a locked cabinet that only the Principal Investigator, Co-Investigators and study coordinator have access to, or will be stored securely electronically.
- The database and computers are password protected and encrypted, and only team members with proper permissions and training have access to data.
- Drawers and offices where study data is kept are locked with only access to appropriate persons.
- Creation of firewalls around data. A firewall is a protection or barrier within a computer to protect the information from being viewed by unauthorized people.

Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.
A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This web site will not include information that can identify you. At most, the Web site will include a summary of results. You can search this Web site at any time.

By signing this document, you give your permission for information gained from your participation in this research study to be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified; all information will be presented as anonymous data.

Complete confidentiality cannot be promised for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

- The research team and investigators at CNRM, USUHS, NICoE, WRNMMC Department of Research Programs;
- The IRBs who are responsible for overseeing the study and ensuring the protection of participants' rights: WRNMMC IRB, USUHS IRB;
- The HJF;
- The NIH
- LMI

Those listed above will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

Data collected during this study will be shared with CNRM. This data will not contain any information that could identify you. As a result, representatives of the CNRM, USUHS, HJF, and NIH may have access to study data for audit purposes.

We may share your data with outside investigators or collaborators but only after all information that can identify you has been removed. This data may be used for a variety of research purposes that we may not be able to specify at this time.

If a study investigator learns that you experience frequent headaches, for example, you may be informed of a study specifically studying "headaches following deployment." If you are interested in participating in additional studies, a study investigator – with your permission – will pass your contact information (email or phone number) on to the relevant investigator. However, if you do not want to participate in other studies, your contact information will not be shared with anyone outside of the immediate research team.

Please check one of the following statements regarding your contact information.

☐ I give permission for investigators to give my contact information (email or phone number) to other investigators who are conducting research studies that may be of interest to me. _____(Initial)

☐ I do not want study investigators to give my contact information (email or phone number) to other investigators._____(Initial)

16. LONG TERM USE OF DATA

The investigator has requested to save selected data collected from your participation in this research study for possible use in future research. You have a number of options with regard to this request. De-identified data may be used for future research if you agree. If the stored data has an identifying link you can request to be contacted and sign a separate consent form to allow the use or available of this data in another study. You may also choose either to not allow any further use of your data or give consent now for the use your data to be used in future studies. This future research may be in the same area as the original study or it may be for a different kind of study. De-identified data will be stored indefinitely.

Any future research using your retained data will require a research protocol for the proposed study approved by an Institutional Review Board (IRB) (a committee responsible for protecting research participants) or other authorized official responsible for protecting human subjects of research. The data protections for privacy and confidentiality described in this consent form will apply to any future use of your stored data.

17. INCIDENTAL FINDINGS

There is a possibility that while reviewing your test results we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by phone. In the case of a potential serious emergency, the researcher

will inform you right away.

You do not have an option to decline receiving information about an incidental finding.

A qualified person (usually a member of the research team) will talk to you if there is an incidental finding.

We will also give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

- An incidental finding may cause you to feel anxious
- Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility. If you are a DoD beneficiary, you will have access to care through standard Military Health System and TRICARE procedures.

18. VOLUNTARY PARTICIPATION

The decision to take part in this research study is completely voluntary on your part. You will be informed if significant new findings develop during the course of this research study that may relate to your decision to continue participation.

19. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

You may withdraw your consent at any time and stop participating in this research study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must contact Dr. Grant Bonavia at 301-319-3713. If you do not follow these procedures, you may experience no health risks, but it is important for the researchers to know your participation status.

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form. If you withdraw from the study, the Principal Investigator may still use the information that was already collected if that information is necessary to complete the study.

The principal investigator of this research study may terminate your participation in this research study at any time if he determines this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

20. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have a research-related injury, notify your Principal Investigator immediately using the contact information in the section below.

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active duty military, dependent of active duty military, retiree), you are authorized space-available medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary. This care includes, but is not limited to, free medical care at DoD hospitals or DoD clinics.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided or paid for by DoD. Unless you are covered by TRICARE, no DoD reimbursement is available if you incur medical expenses to treat research- related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights.

21. CONTACT INFORMATION:

Principal Investigator (PI)
The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Principal Investigator: Dr. Grant H. Bonavia, MD, PhD Phone: 301-319-3713
Mailing Address: National Intrepid Center of Excellence (NICoE) Walter Reed National Military Medical Center
4860 South Palmer Road, Bethesda, MD 20889

Study Coordinator Phone: 301-295-4248

Mailing Address: Uniformed Services University of the Health Sciences Center for Neuroscience and Regenerative Medicine
6720B Rockledge Drive, Bethesda, MD 20817

WRNMMC Human Research Protection Program (HRPP) Office
The Human Research Protection Program Office Point of Contact and/or Human Protections Administrator (HPA) will be available to answer questions or discuss concerns you may have about this research study.

Human Protections Administrator/HRPP POC Phone: 301-295-8239.

Staff Judge Advocate
Phone: 301-295-2215.

Institutional Review Board (IRB) Office
If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the IRB Office at:
Phone: 301-295-8239

Mailing Address: Walter Reed National Military Medical Center IRB Building 17B, 3rd floor, Suite C, 4494 North Palmer Road, Bethesda, MD 20889

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND,

ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL PHYSICIAN OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

Please initial the sentences that reflect your choices, and then sign below:

_____I do not authorize the storage of data collected as a part of this study for future use in research studies.

_____I authorize the storage of data collected as a part of this study for future use in research studies.

With regard to future research studies done on stored data that has a link to my personal identity.

_____I do not wish to be notified by investigators in the event of research findings of potential impact to my family members or myself.

_____I wish to be notified by investigators in the event of research findings of potential impact to my family members or myself. I agree that my current principal investigator may use any appropriate identifier to locate me in the future.

In addition, you may provide consent for study staff to provide your name and contact information (email, phone number) to the TROOPS staff. Your information will be sent securely and will not be shared with anyone else. This is voluntary. Please indicate your choice below.

With regard to sharing my contact information with TROOPS CNRM investigators and approved study staff:
_____YES, I authorize the sharing of my contact information with TROOPS staff
_____NO, I do not authorize sharing of my contact information with TROOPS staff.

SIGNATURE OF PARTICIPANT

By signing below, I agree that I have been provided time to read the information describing the research study in the consent form. The content and meaning of this information has been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research participant.

_____
Printed Name of Participant

_____ _____
Signature of Participant Date

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT
(Can only be signed by an investigator or staff approved to administer consent)

_____
Printed Name of Administering Individual

_____ _____
Signature of Administering Individual Date

AUTHORIZATION TO USE OR DISCLOSE (RELEASE) HEALTH INFORMATION THAT IDENTIFIES YOU FOR A RESEARCH STUDY
Protocol # 18-03690

Principal Investigator (PI) Name and Rank: Grant Bonavia, MD PhD

Corps and Service/Organization: National Intrepid Center of Excellence (NICoE) – Research / Imaging and Measurement; Walter Reed National Medical Military Center (WRNMMC)

Title of Research Study: Imaging [^{18}F]PI-2620 and Florbetaben F18 in military service members with blast-related mild traumatic brain injury

I. Purpose of this Document
An Authorization is your signed permission to use or disclose your health information. The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, as implemented by the Department of Defense (DoD), permits the Military Health System (MHS) to use or disclose your health information with a valid Authorization. The MHS is defined as all DoD health plans and DoD health care providers that are organized under the management authority of, or in the case of covered individual providers, assigned to or employed by, the Defense Health Agency (DHA), the Army, the Navy, or the Air Force. A valid Authorization must include the core elements and required statements as contained in this document.

Please read the information below and ask questions about anything you do not understand before deciding to give permission for the use and disclosure of your health information.

II. Authorization
The following describes the purposes of the requested use and disclosure of your health information:
This study, "Imaging [^{18}F]PI-2620 and Florbetaben F18 in military service members with blast related mild traumatic brain injury," is aiming to use imaging and neuropsychological tests to assess the effects of blast-related mTBI on changes in thinking and brain structure in military service members. By using these techniques, we aim to see what areas of the brain might be damaged or functioning differently, and if we can use a radiotracer to identify CTE or neurodegeneration. Your health information that is collected will be used for the purpose of conducting this study.

A. What health information will be used or disclosed about you?
The following information may be collected by the research team for the purposes of this study:
· Name, address, telephone number, social security number, birthdate
· Medical record
· Medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc)
· PET scans, MRI scans
· Mental health history
· Alcohol or substance abuse history
· Neuropsychological tests and questionnaires or data from already completed measures
· Other information gathered as part of this study

B. Who will be authorized to use or disclose (release) your health information?
The following people or organizations are authorized to use or disclose (release) your health information:

- The Principal Investigator, Dr. Bonavia, and the research team
- The Military Health System (MHS)
- NICoE, WRNMMC, Walter Reed Army Institute of Research (WRAIR)
- The Defense Health Agency (DHA)

C. Who may receive your health information?
The following people or organizations may receive your health information or research record for purposes related to conducting the study (such as for legal or regulatory purposes):

- The CNRM, USUHS, HJF
- The NIH, the FDA
- NICoE, WRNMMC
- Life Molecular Technologies (LMI)
- The United States Department of Health and Human Services (HHS), the Office of Human Research Protection (OHRP), the HHS Office for Civil Rights
- The institutional review board which oversees this study, WRNMMC IRB. The IRB ensures participant safety and protects participants' rights.

D. Is your health information requested for future research studies?
Yes, your health information *is* requested for future research studies as specified below:
If possible, the study team would like to contact you in the future after this study has ended to perform longitudinal research using your information, and potentially having you come in for future visits so we may learn more about the long-terms effects of mTBI and blast. Your health information will not be used for future research studies unless you give your permission by initialing your choice below:

_____I give permission to use my health information for future research studies

_____I *do not* give permission to use my health information for future research studies

E. Can you access your health information during the study?
You may have access to your health information at any time, unless your identifiers are permanently removed from the data.

F. Can you revoke this Authorization?
• You may change your mind and revoke (take back) your Authorization at any time. However, if you revoke this Authorization, any person listed above may still use or disclose any already obtained health information as necessary to maintain the integrity or reliability of this research.
• If you revoke this Authorization, you may no longer be allowed to participate in this research study.
• If you want to revoke your Authorization, you must write to: Grant Bonavia, MD, PhD
National Intrepid Center of Excellence
Walter Reed National Military Medical Center 4860 South Palmer Road, Bethesda, MD 20889

G. Does this Authorization expire?
No, it does not expire.

H. What happens if you do not grant this Authorization?
If you choose not to grant this Authorization there will be no impact on your ability to receive care at this facility but you will not be eligible to participate in this research study.

I. What else may you want to consider?
• No publication or public presentation about the research described above will reveal your identity without another signed Authorization from you.
• If all information that does or can identify you is removed from your health information, the remaining de-identified information will no longer be subject to this Authorization and may be used or disclosed for other purposes.
• In the event your health information is disclosed to an organization that is not covered by HIPAA, the privacy of your health information cannot be guaranteed.

Signature of Research Participant or Personal Representative:

Your signature acknowledges that:

- You authorize the MHS to use and disclose your health information for the research purposes stated above.
- You have read (or someone has read to you) the information in this Authorization.
- You have been given a chance to ask questions, and all of your questions have been answered to your satisfaction.

_____ _____
Participant Signature Date

_____
Participant Printed Name