UNIVERSITY OF CALIFORNIA, SAN DIEGO
CONSENT TO PARTICIPATE IN RESEARCH

1. Study Title and Number

Title: Entire-body PET Scans for Multiple Sclerosis (EPSMS)
Study # 805653/ BHA-2020-11

2. Principal Investigator

Carl Taswell, MD, PhD, Affiliate, Department of Radiology, UCSD School of Medicine

3. Principal Investigator Phone Number, Research Team Number, and Emergency Contact Number

Phone: 949-481-3121
Email: ctaswell@health.ucsd.edu or ctaswell@BrainHealthAlliance.org

4. Study Sponsor

Brain Health Alliance (BHA), the study sponsor, is collaborating with UC San Diego to conduct this research study. Avid Radiopharmaceuticals has agreed to fund the first 20 doses of Amyvid for the pilot phase of the clinical trial. Research study doctors and staff do not receive any direct income from the study sponsor or supporters. The supporters of this study may be changed or additional sponsors and supporters may be added, especially if the initial pilot study is extended to a multi-year clinical trial with a greater number of study participants. Study costs are paid by Brain Health Alliance.

5. Study Overview

This research study is being conducted to examine whether recent state-of-the-art PET-CT scanners, such as the United Imaging uEXPLORER and the Siemens Biograph Vision, with much greater sensitivity and resolution, can serve as improved imaging devices to monitor better the demyelination, or damage to the sheath around the nerves, and remyelination, or renewal of the sheath around the nerves, that may occur in the white matter of the nervous system of persons with multiple sclerosis when compared to healthy subjects. This demyelination and remyelination may correlate with the relapses and remissions of multiple sclerosis.

The study will be managed by experienced researchers at Brain Health Alliance (BHA), and the PET scans will be performed by experienced physicians and technologists at the collaborating medical centers. The questions addressed in the study will ask whether PET imaging with an entire-body PET scanner and the Amyvid imaging dye to monitor demyelination and remyelination in multiple sclerosis will ultimately help your doctor to treat you, manage your illness, and benefit your health. However the PET scanner only takes a picture and provides information. It does not constitute a treatment by itself. The Amyvid imaging dye is neither known nor presumed to be a treatment of any kind.

We are inviting you to participate in a research study because you have been diagnosed with multiple sclerosis, have been told by your neurologist that you have a severe disability score (> or = 5.5 on the Kurtzke scale), and are between the ages of 25 and 55, inclusive. Alternatively, you are between the ages of 25 and 55 inclusive and have volunteered to participate as a healthy research subject.

This form explains the research so that you may make an informed decision about participating.

- Research is voluntary - whether or not you participate is your decision. You can discuss your decision with others (such as family, friends or another physician).

- You can say yes, but change your mind later.
- If you say no, we will not hold your decision against you.
- You can say no even if the person inviting you is part of your healthcare team.
- Your decision will not affect your health care or other benefits you may be entitled to.
- Please ask the study doctor or study team questions about anything that is not clear, and feel free to ask questions and mention concerns before, during, and after the research.
- You may consult with friends, family, a personal doctor, or anyone else before deciding whether or not to be in the study.
- You will be given a copy of this consent form and the Participant's Bill of Rights.

If you have any further questions or concerns about your rights as a research subject, please contact your research doctor, UCSD'S Human Research Protections Program at 858-246-HRPP (858-246-4777), or Brain Health Alliance, the sponsor.

The purpose of this research study is to evaluate whether entire-body PET-CT scans can improve imaging in multiple sclerosis patients in order to improve patient care. These PET-CT scanners may be a better tool for imaging the white matter of the brain, spinal cord, and peripheral nerves.

These new FDA-approved PET-CT scanners are now able to scan most if not all of the human body at the same time. They are also much more efficient that previous PED-CT scanners and have the potential to make a big impact in clinical care and medical research. All participants in the EPSMS pilot study will receive the same kind of PET-CT scan with the same imaging dye, an FDA-approved radiopharmaceutical called Amyvid. This single scan will be performed at one of the possibly several collaborating medical imaging centers and may take several hours of your time. All participants may accept or decline to be informed of the results from this PET-CT scan. If you do wish to be informed of the scan results, then you must also agree to participate in educational counseling sessions with questionnaires (ie, psychological screening tests) before and after the PET scan. Each of these sessions may also take several hours of your time. If you do not wish to be informed to be informed of the PET scan results, then you will not be required to attend the educational counseling sessions with the questionnaires before and after the PET scan.

The most common risks or discomforts of this study are the risks from radiation exposure, the infusion of the Amyvid dye, and the discomfort of lying still while the imaging is taking place.

The most serious risks include exposure to radiation from a molecular imaging scan with a PET-CT scanner. More information about this risk is explained on page 5. If you are especially concerned with radiation exposure, or if you have had a large number of X-rays or imaging scans already, discuss this risk with a study doctor or your regular doctor.

A complete listing of possible risks and discomforts associated with this study can be found in Section 9 of this document.

We cannot promise any benefit to you or to others from you participating in this research. However, possible benefits include, if you participate in the disclosure of imaging results to you and your treating physician, your direct care provider may receive the results of your PET-CT scan and may use that information in supporting your future care. Additionally, you may benefit from increased knowledge about the influence of the PET scan on clinical decision making and medical outcomes when the study results become available. In the future, the knowledge learned during this study could help guide the appropriate use of PET scan imaging in patients whose conditions are difficult to diagnose and monitor.

The alternative to being in this study is not to participate. PET scans with Amyvid can be obtained outside of the study, but it is unlikely that the test could be performed with an entire-body PET-CT scanner unless it is done as a part of the study.

More detailed information about this research study is provided below.

6. Whom can I talk to if I have questions?

If during your participation in the study you have questions or concerns, or if you think the research has hurt you, contact the research team at the numbers listed in Section 3 on the first page of this form. You should not agree to participate in this study until the research team has answered any questions you have about the study, including information contained in this form.

If before or during your participation in the study you have questions about your rights as a research participant, or you want to talk to someone outside the research team, please contact:

- UC San Diego Office of IRB Administration at 858-246-4777 or irb@ucsd.edu

7. How many people will take part?

We plan to study 10 people with multiple sclerosis and 10 healthy individuals to start. The research is a pilot study, and will include additional people across all locations if the pilot study is successful.

8. What happens if I take part in the research?

Here is what will happen to you if you agree to be in this study:

- Information about you, your health, and your PET scan imaging will be collected for up to one year.
- The research team will need to collect your name, phone number, street address, social security number, and date of birth to allow the researchers to contact your health care providers about your medical care before and after the PET scan. They will ask you to sign a release of information form to attain a copy of your medical records. Only trained research staff at BHA and the collaborating medical imaging center at UCSD will have access to your personal information.
- Participate in a single scan with an entire-body PET-CT scanner and Amyvid radiopharmaceutical. You must be able to lie on your back in a long PET-CT scanner for the duration of the scan, which will be approximately 10 to 20 minutes.
- The Amyvid dye will be given to you through an intravenous (IV) infusion. Therefore, before the scan begins, you will have an IV line inserted.
- If you do agree to participate, you will advise us of a friend or family member who has agreed to assist and accompany you throughout the study, especially to the imaging center at the time of the PET scan.
- If you wish to be informed of the results of the PET scan, then you also agree to participate in the educational counseling sessions with questionnaires before and after the PET scan.
- You allow your PET scan and any other data collected from the questionnaires, which will be stripped of all personal identifying information, to be analyzed for the current EPSMS research project and also archived in a locked system at BHA for future research.

Please note that both the PET-CT scanner and the Amyvid dye used for the scan are already approved for use by the FDA.

As you read this form, ask questions if something is not clear.

There will be one visit to the site where the PET-CT scanner is located on UCSD campus, where the single PET-CT scan will be obtained. If you have asked to be informed of the results of the scan, then there will be a pre-scan and post-scan appointment. These will include filling out questionnaires, and may take an additional two hours.

Any biospecimens, such as blood or urine, collected from you by UC San Diego Health Imaging and Radiology for this imaging study and/or information obtained from your biospecimens may be used in this research or other research, and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them. There is no specific plan right now to ask for any biospecimens from you for this study.

You will be asked to sign and date a separate form for UC San Diego Health authorizing access, use, and creation, or disclosure of health information about you. Members of the research team and other staff or representatives of UC San Diego Health whose work is related to the research or to protecting your rights and safety. This consent form and some details of your study participation will be noted in your UCSD medical record. People involved with your medical care and insurance at UCSD Health or other organizations may become aware of these details.

There are no long-term follow-up precedures.

PET-CT machines are able to both perform a CT (computerized tomography, a complex type of X-ray) and to detect special chemicals that are able to show bodily functions to make pictures of the inside of your body. During the scanning, you will lie on a long narrow couch for 10-20 minutes while the machine gathers data. You will not feel anything while the data is being collected. You will also hear noises that are from the scanner.

Since the PET-CT scanner is an X-ray, you will be exposed to the radiation from that portion of the scan. In addition, for the PET portion of the scan, you will also be exposed to radioactive materials that allow the machine to visualize the areas of the body that the materials detect.

The radioactive material used in this study may affect a baby before the baby is born. As a result, those able to become pregnant should not be in this study if they are:

- pregnant,
- breast-feeding, or
- trying to become pregnant.

If you are of child-bearing age, you must be willing to take a pregnancy test at the time of the PET-CT scan, and you will be excluded from the study if you are pregnant. If you are able to become pregnant, you should use birth control for the three months prior to your PET-CT scan and for one month afterwards. Hormonal methods (birth control pill, etc.), double-barrier methods (condoms with spermicidal, sponge with spermicidal, or diaphragm with spermicidal), or not having sex may be used. Your doctor will discuss these with you.

If you are able to cause a pregnancy, you should not have unprotected sex with someone who is able to become pregnant during the month after the PET-CT scan. If your partner(s) is/are able to become pregnant, you and your partner(s) should use birth control for the month month afterwards. Hormonal methods (birth control pill, etc.), double-barrier methods (condoms with spermicidal, sponge with spermicidal, or diaphragm with spermicidal), or not having sex may be used. Your doctor will discuss these with you.

If you become pregnant or think you might be pregnant during the month following the PET-CT scan, you must inform the Study Doctor immediately. Your Study Doctor will want to follow the pregnancy and collect information about the outcome of the pregnancy.

You should not donate sperm/eggs during the month after the PET-CT scan.

9. What are the risks and possible discomforts?

Participation in this study may involve risks or discomforts. During your participation in this research study, you will be exposed to radiation from a molecular imaging scan with a PET-CT scanner. The total exposure resulting from these imaging studies is calculated to be approximately 7 mSv. This amount is more than you would receive from one year of natural exposure in the San Diego area, which is approximately 1.6 mSv. Cumulative exposure from radiation may increase your risk of developing certain types of cancer in the future.

The PET imaging test performed with the radiopharmaceutical Amyvid (F18-florbetapir) as described in this consent form is *not* experimental and has been safely used in clinical practice since the imaging agent was first approved by the FDA in 2012. However, there are risks associated with this imaging test that will be discussed with you and also addressed again in a separate consent form at the collaborating medical center where the imaging test will be performed with the entire-body PET scanner. These risks include exposure to very low doses of radiation, which is much lower than the amount for a regular diagnostic CT scan.

During the scan, you will be in an enclosed space and this may cause some people to experience discomfort or claustrophobia (fear or anxiety when in a small confined space). The injection of the radiotracer may cause pain at the injection site, and rarely, may cause an allergic reaction. The most common adverse side effect has been headache affecting less than 2% of persons who are injected with Amyvid and imaged with a PET scanner. You will be carefully monitored to minimize these effects in the event that you experience any of them.

Also, the PET scan may reveal incidental findings and/or suspicious findings of unclear cause which may need further follow-up procedures. Medical follow-up may include doctor's visits, more scans or surgery and may expose you to additional risks from the follow-up procedures. Your participation in this study is voluntary. You do not have to participate in this study if you do not wish to do so. There may be other choices available to you. You will not lose any services, benefits, or rights you would normally have if you choose not to participate in this pilot study.

Another known risk of participating in this type of research study is the possibility of unintentional release of your personal health information. The research team takes extra precautions to lessen and minimize this risk. For the research study database, you will be identified only by a unique number. Your name and other identifying personal information will not be included in the research study database. Any identifying personal information will be accessed only by trained research staff personnel who need it to make requests for health care information obtained from your health care providers for which you must sign permission for them to release any records to the research study. An example of such information would be your multiple sclerosis disability scores and clinic notes from your neurologist who is caring for your illness. This information will be recorded in the research study database with only your unique code number, and will have your name and identifying information removed from the information prior to entry in the research database. Any new important information that is discovered during the research study and which may influence your willingness to continue participation in the study will be made available to you.

Risks of Radiation Exposure:
Please see the above paragraphs on the risks of this study. During your participation in this research study, you will be exposed to radiation from scheduled imaging scans. The total exposure resulting from these imaging studies is calculated to be approximately 7 mSv. This amount is more than you would receive from one year of natural exposure in the San Diego area, which is approximately 1.6 mSv. Cumulative exposure from radiation may increase your risk of developing certain types of cancer in the future.

The principal investigator for this research study has determined and verified that some of the imaging scans prescribed for this study might typically be performed as part of the standard medical care required to adequately monitor your current illness. If you are especially concerned about radiation exposure, or you have had many x-rays and/or imaging scans already, you should discuss this with the study doctor or your regular doctor.

Possible Unknown Risks: In addition, there might be risks that we cannot predict at this time. These unknown risks may be temporary, mild, and last only while you are actively participating in the research, or they may be serious, long-lasting, and may even cause death. You will be informed of any new findings that might affect your health or welfare, or might affect your willingness to continue in the research.

10. How will information about me be protected?

While we cannot guarantee complete confidentiality, we will limit access to information about you. Only people who have a need to review your information, documents, or specimens will have access. These people might include:

- Members of the research team and other staff or representatives of UCSD whose work is related to the research or to protecting your rights and safety.
- Representatives of the study sponsor or product manufacturer
- Representatives of Federal and other regulatory agencies who make sure the study is done properly and that your rights and safety are protected.

Study information will be labeled with a code instead of your name or other information that can easily identify you. The record linking your identifying information (name, address, etc.) and the code will be kept separate from the rest of the study information.

This consent form and some details of your study participation will be noted in your UC San Diego Health record. If you do not currently have a UC San Diego Health record, one will be developed for you. People involved with your medical care and insurance at UC San Diego or other organizations may become aware of these details. Federal and state privacy laws give patients the right to access information about their care and treatment contained in their medical record. During this study, you may not be able to access certain information related to this study in your UC San Diego Health record until the study is complete to ensure that the study remains unbiased. By consenting to participate in this study, you are also consenting to this possible temporary withholding of your research records.

The results of this study may be published once the study is completed. However, we will keep your name and other identifying information confidential. We expect this study will be completed in approximately one year. This is only an estimate and the actual time to complete the study may be longer or shorter depending on a number of factors.

You will be asked to sign separate UC Health Insurance Portability and Accountability Act (HIPAA) Research Authorization form to use and disclose (share) your health information that identifies you for the purposes of this research study (see the separate authorization form for more information). Your permission as described in this informed consent and authorization form does not have an automatic expiration date.

11. Will I need to pay to participate in the research?

There will be no cost to you for participating in this study. There may be expenses for parking or transportation to the medical center. You and/or your health plan/insurance company will need to pay for all costs of treating your condition while in this study.

The Amyvid dye used for your scan will be supplied at no cost while you take part in this study. The cost of getting the Amyvid ready and giving it to you is also provided at no cost

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your condition while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no cost. Before you decide to be in the study, you should check with your health plan/insurance company to find out exactly what they will pay for.

12. What if I agree to participate, but change my mind later?

You can stop participating at any time for any reason, and it will not be held against you. Your choice will not affect any treatment relationship you have with healthcare providers at UC San Diego Health or any services you receive from them. No matter what you decide, there will be no penalty to you. You will not lose medical care or any legal rights.

The decision to participate is voluntary. You can choose not to participate or you may decide to volunteer now and then later withdraw from the study for any reason at any time. You can inform the study team at BHA in writing at the address listed on the first page of this form. Any data collected prior to your withdrawal from the study will belong to the clinical trial, and may be used for research by BHA. If you stop participating, we may not be able to remove the information we have already collected about you or specimens we have already collected from you. The study doctor or sponsor can stop your participation at any time without your consent for the following reasons: if it appears to be medically harmful to you, if you fail to follow directions for participating in the study, if it is discovered that you do not meet the study requirements, if the study is canceled, or for administrative reasons.

13. What will happen to information collected from me?

The data we collect with your identifiable information (for example, your name, medical record number, or date of birth) as a part of this study may be used to answer other research questions or may be shared with other investigators for other research. If we do so, we will remove all identifiable information before use or sharing. Once identifiers have been removed, we will not ask for your consent for the use or sharing of your data in other research.

While your privacy and confidentiality are very important to us and we will use safety measures to protect it, we cannot guarantee that your identity will never become known.

14. What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for:

We will expect you to participate in the pre-scan and post-scan educational sessions to be eligible to receive your scan results.

15. Will I be compensated for participating in the research?

We will not pay you to take part in this study or pay for any out of pocket expenses related to your participation, such as travel costs.

16. What else is important for me to know?

You will be provided any clinically relevant information that may pertain to your health if you have asked to receive your results and participate in the pre-scan and post-scan questionnaires.

The risks of participating in this study are minimal. However, If you are injured as a result of being in this study, UC San Diego will provide necessary medical treatment. The costs of the treatment may be covered by the University of California or the study sponsor, or billed to you or your insurer just like other medical costs, depending on a number of factors. The University and the sponsor do not normally provide any other form of compensation for injury. For more information about this, you may contact the UC San Diego Office of IRB Administration at 858-246-4777 or irb@ucsd.edu

If you receive Medicare benefits, the sponsor, Brain Health Alliance, is required by law to report payments made to you for treatment, complications, and injuries that arise from this study. Information will be provided to the Centers of Medicare and Medicaid Services and its agents and/or contractors for this purpose. UC San Diego will provide the Sponsor with your name, date of event and health identification number (if not available, then Social Security number) only for Medicare beneficiaries that have had a study related injury for which the sponsor has issued reimbursement to the University.

If you have questions, concerns, or complaints regarding your participation in this study, you should contact your treating or referring physician and also the principal investigator, Dr. Carl Taswell, identified on the first page of this consent form. If you have any questions about your rights as a clinical trial research subject, and/or concerns or complaints regarding this pilot study, you should write to Dr. Carl Taswell, Brain Health Alliance, 8 Gilly Flower St, Ladera Ranch, CA 92694. You may also email him at ctaswell@BrainHealthAlliance.org or call him at 1(949)481- 3121.

Additional information to help you understand clinical trial research can be found online at https://clinicaltrials.gov/ct2/about-studies/learn. A description of this clinical trial will be available on ClinicalTrials.gov as required by US Federal Law. The EPSMS clinical trial has been assigned the identifier NCT04390009 by ClinicalTrials.gov. This website will not include any information that can identify you. At most, the website will include a summary of the results. You can search this website at any time. You may also contact the UC San Diego Office of IRB Ad- ministration at 858-246-4777 or irb@health.ucsd.edu to inquire about your rights as a research subject or to report research-related problems.

17. Additional Choices to Consider

PET Scan Results

If you agree to participate in the EPSMS clinical trial, and you do plan to complete a PET imaging test with an entire-body PET scanner and the Amyvid imaging dye, please let us know if you wish to be informed of your PET scan results with regard to amyloid in the grey matter of the brain, myelin in the white matter of the brain and nervous system, both amyloid and myelin, or neither. If you wish to be informed of any results, regarding either amyloid and/or myelin, then you must also spend some time (both before and after the PET scan) talking with a doctor who will provide the necessary education and counseling with respect to disclosure of the imaging results from the PET scan.

_____(insert initials) YES, I wish to be informed about the results from my PET scan concerning the white matter of the brain and nervous system related to myelin.

_____(insert initials) YES, I wish to be informed about the results from my PET scan concerning the grey matter of the brain related to amyloid.

_____(insert initials) NO, I do not want to be informed about the results from my PET scan.

The study team would like your permission to contact you about participating in future studies. You may still join this study even if you do not permit future contact. You may also change your mind about this choice. Please initial your choice below:

_____YES, you may contact me

_____NO, you may NOT contact me

UNIVERSITY OF CALIFORNIA, SAN DIEGO

CONSENT TO PARTICIPATE IN RESEARCH

Signature Block for Adults Able to Provide Consent

Participant

I have received a copy of this consent document and a copy of the "Experimental Participant's Bill of Rights" to keep. I agree to participate in the research described in this form.

Printed Name of Participant

Signature of Participant Date

Person Obtaining Consent

I document that:

- *I (or another member of the research team) have fully explained this research to the participant.*
- *I have personally evaluated the participant's understanding of the research and obtained their voluntary agreement.*

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent Date

Witness (if applicable)

I document that the information in this form (and any other written information) was accurately explained to the participant. The participant appears to have understood and freely given consent to join the research.

Printed Name of Witness

Signature of Witness Date

Experimental Participant's Bill of Rights

Every individual asked to participate in a research study has the right to be:

1. Informed about the nature and purpose of the study.

2. Provided an explanation of the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. Given a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. Informed about any benefits that would reasonably be expected from the participation in the study, if applicable.

5. Informed about of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. Told of the types of medical treatment, if any, available if complications should arise.

7. Provided an opportunity to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. Informed that individuals can refuse to participate in the research study. Participation is voluntary. Research participants may refuse to answer any question or discontinue their involvement at any time without penalty or loss of benefits to which they might otherwise be entitled. Their decision will not affect their right to receive the care they would receive if they were not in the experiment.

9. Provided a copy of the signed and dated written consent form and a copy of this form.

10. Given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study contact the researchers listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research participant, please contact:

- UC San Diego Office of IRB Administration at irb@ucsd.edu or 858-246-4777