

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)

Approval Period: 04/22/2020 - 09/24/2020

Modification

1. Summarize your proposed changes.

We are making minor modifications to clarify the device descriptions, combining all the MRI receive coil components into the description of the whole MRI system. We are also removing devices that were previously erroneously marked as IDE exempt devices after discussion with the IRB, as these devices are not being studied.

Total number of participants study-wide are 34 (34 reported last year). Target is 0-20/year.

There will be no change to the consent form that was last approved (01/28/2020), but our plan is to still re-consent all participants going forward that have not already completed this consent form.

2. Indicate Level of Risk

No Change

3. Update the Conflict of Interest (COI) section if any changes in COI have been made since the last protocol submission.

N Is there a change in the conflicting interest status for any existing personnel on this protocol?

Protocol Director

Name Brian A Wandell		Degree (Program/year if student) PhD		Position, e.g. Assistant Professor, Resident, etc. Professor
Department Psychology	Mail Code 2130	Phone (650) 725-2466	Fax	E-mail wandell@stanford.edu
CITI Training current				Y

Admin Contact

Name Lee Michael Perry		Degree (Program/year if student) BA		Position, e.g. Assistant Professor, Resident, etc. Lab Manager
Department Psychology	Mail Code 2130	Phone (650) 725-0051	Fax (801) 409-3254	E-mail lmperry@stanford.edu
CITI Training current				Y

Investigator

Name Adam Bruce Kerr		Degree (Program/year if student) PhD		Position, e.g. Assistant Professor, Resident, etc. Sr Research Engineer
Department Electrical Engineering - Information Systems Laboratory	Mail Code 9510	Phone (650) 725-0051	Fax	E-mail akerr@stanford.edu
CITI Training current				Y

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)

Approval Period: 04/22/2020 - 09/24/2020

Other Contact

Name Laima Baltusis		Degree (Program/year if student) PhD		Position, e.g. Assistant Professor, Resident, etc. Science & Engineering Assoc
Department Cognitive and Neurobiological Imaging Center	Mail Code 2130	Phone (650) 725-8382	Fax	E-mail laimab@stanford.edu
CITI Training current				Y

Academic Sponsor

Name		Degree (Program/year if student)		Position, e.g. Assistant Professor, Resident, etc.
Department	Mail Code	Phone	Fax	E-mail
CITI Training current				

Other Personnel

Name Hua Wu		Degree (Program/year if student) PhD		Position, e.g. Assistant Professor, Resident, etc. Sr. Research Engineer
Department Cognitive and Neurobiological Imaging Center	Mail Code	Phone (650) 723-0967	Fax	E-mail huawu@stanford.edu
CITI Training current				Y

Participant Population(s) Checklist

Yes/No

- | | |
|--|---|
| • Children (under 18) | N |
| • Pregnant Women and Fetuses | N |
| • Neonates (0 - 28 days) | N |
| • Abortuses | N |
| • Impaired Decision Making Capacity | N |
| • Cancer Subjects | N |
| • Laboratory Personnel | Y |
| • Healthy Volunteers | Y |
| • Students | Y |
| • Employees | Y |
| • Prisoners | N |
| • Other (i.e., any population that is not specified above) | N |

Study Location(s) Checklist

Yes/No

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

- Stanford University Y
- Clinical & Translational Research Unit (CTRU)
- Stanford Hospital and Clinics
- Lucile Packard Children's Hospital (LPCH)
- VAPAHCS (Specify PI at VA)
- Other (Click ADD to specify details)

General Checklist

Multi-site Yes/No

- Is this a multi-site study? A multi-site study is generally a study that involves one or more medical or research institutions in which one site takes a lead role.(e.g., multi-site clinical trial) N

Collaborating Institution(s) Yes/No

- Are there any collaborating institution(s)? A collaborating institution is generally an institution that collaborates equally on a research endeavor with one or more institutions. N

Cancer Institute Yes/No

- Cancer-Related Studies (studies with cancer endpoints), Cancer Subjects (e.g., clinical trials, behavior/prevention) or Cancer Specimens (e.g., blood, tissue, cells, body fluids with a scientific hypothesis stated in the protocol). N

Clinical Trials Yes/No

- Investigational drugs, biologics, reagents, or chemicals? N
- Commercially available drugs, reagents, or other chemicals administered to subjects (even if they are not being studied)? N
- Investigational Device / Commercial Device used off-label? Y
- IDE Exempt Device (Commercial Device used according to label, Investigational In Vitro Device or Assay, or Consumer Preference/Modifications/Combinations of Approved Devices) N
- Will this study be registered on# clinicaltrials.gov? (See Stanford decision tree) N
- Is Stanford responsible for ClinicalTrials.gov registration? (See Stanford decision tree) NCT# N

Tissues and Specimens Yes/No

- Human blood, cells, tissues, or body fluids (tissues)? N

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

- Tissues to be stored for future research projects? N
- Tissues to be sent out of this institution as part of a research agreement? For guidelines, please see <https://sites.stanford.edu/ico/mtas> N

Biosafety (APB)**Yes/No**

- Are you submitting a recombinant DNA vector or Human Gene Transfer investigation using biological agents? If yes, please complete and attach the Gene Transfer Protocol Application Supplemental Questions to section 16 of the eProtocol application. N
- Are you submitting a Human study using biohazardous/infectious agents? If yes, refer to the <http://www.stanford.edu/dept/EHS/prod/researchlab/bio/index.html> Administrative Panel on BioSafety website prior to performing studies. N
- Are you submitting a Human study using samples from subjects that are known or likely to contain biohazardous/infectious agents? If yes, refer to the <http://web.stanford.edu/dept/EHS/prod/researchlab/bio/index.html> Administrative Panel on BioSafety website prior to performing studies. N

Human Embryos or Stem Cells**Yes/No**

- Human Embryos or Gametes? N
- Human Stem Cells (including hESC, iPSC, cancer stem cells, progenitor cells) N

Veterans Affairs (VA)**Yes/No**

- The research recruits participants at the Veterans Affairs Palo Alto Health Care System(VAPAHCS). N
- The research involves the use of VAPAHCS non-public information to identify or contact human research participants or prospective subjects or to use such data for research purposes. N
- The research is sponsored (i.e., funded) by VAPAHCS. N
- The research is conducted by or under the direction of any employee or agent of VAPAHCS (full-time, part-time, intermittent, consultant, without compensation (WOC), on-station fee-basis, on-station contract, or on-station sharing agreement basis) in connection with her/his VAPAHCS responsibilities. N
- The research is conducted using any property or facility of VAPAHCS. N

Equipment**Yes/No**

- Use of Patient related equipment? If Yes, equipment must meet the standards established by Hospital Instrumentation and Electrical Safety Committee (650-725-5000) N
- Medical equipment used for human patients/subjects also used on animals? Y
- Radioisotopes/radiation-producing machines, even if standard of care? http://www.stanford.edu/dept/EHS/prod/researchlab/radlaser/Human_use_guide.pdf More Info N

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

Payment**Yes/No**

- Subjects will be paid/reimbursed for participation? See payment considerations.

N

Funding**Yes/No**

- Training Grant?
- Program Project Grant?
- Federally Sponsored Project?
- Industry Sponsored Clinical Trial?

N

N

N

N

Funding

NONE

Funding - Grants/Contracts**Funding - Fellowships****Gift Funding****Dept. Funding****Other Funding****Resources :****a) Qualified staff.****Please state and justify the number and qualifications of your study staff.**

All members of the research team are CITI certified and have completed HIPAA training. Those members of the research team that will be running subjects at the facility have completed the appropriate safety training courses required to scan subjects.

b) Training.**Describe the training you will provide to ensure that all persons assisting with the research are informed about the protocol and their research-related duties and functions.**

Members of the research team include the Research Director for the CNI and the Facility Manager. They will provide the training to other users of the CNI facility. Each has more than fifteen years of experience with MR equipment and will be further trained in the equipment use by General Electric (who manufacture the MR scanner), as needed.

c) Facilities.

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

Please describe and justify.

The Cognitive and Neurobiological Imaging facility comprises an MR scanner (a 3T Ultra-High Performance scanner manufactured by GE Healthcare) and physiological monitoring equipment. The CNI will be the primary site for data acquisition and analysis.

The Lucas Center facility includes two 3T MR scanners: one is a GE 3T MR750, the other is a GE 3T Premier system. These will be the only MR systems at Lucas used for data acquisition. There are other MR systems at Lucas including a 3T PET/MR system and a 7T MR system but neither of these nor any other imaging system at Lucas will be used for this project.

d) Sufficient time.

Explain whether you will have sufficient time to conduct and complete the research. Include how much time is required.

The CNI is a Stanford service center that is funded by user fees. We anticipate continuing development of MR methods for as long as the service center is in operation, so there is no anticipated end date.

e) Access to target population.

Explain and justify whether you will have access to a population that will allow recruitment of the required number of participants.

Normal volunteers will be recruited from CNI staff and the Psychology department's volunteer database.

f) Access to resources if needed as a consequence of the research.

State whether you have medical or psychological resources available that participants might require as a consequence of the research when applicable. Please describe these resources.

Any potential incidental findings will be reviewed by a Neuroradiologist from the Stanford Department of Radiology.

g) Lead Investigator or Coordinating Institution in Multi-site Study.

Please explain (i) your role in coordinating the studies, (ii) procedures for routine communication with other sites, (iii) documentation of routine communications with other sites, (iv) planned management of communication of adverse outcomes, unexpected problems involving risk to participants or others, protocol modifications or interim findings.

1. Purpose**a) In layperson's language state the purpose of the study in 3-5 sentences.**

Understanding how brain systems guide human performance is an increasingly important part of many scientific disciplines and measurements of the normally functioning human brain are revolutionizing many parts of the social sciences. The principles of brain function now find applications in explaining many phenomena in the fields of Education, Psychology, Psychiatry, Neurology, Economics, Business and Law.

This protocol is intended to support the development and performance validation of new MR methods and experimental designs that will be used by researchers in these fields. Some

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

of these new methods are developed locally by the CNI, while others are made available as works-in-progress from GE Healthcare or other researchers via the GE Healthcare software-sharing portal. Before making new methods available to other researchers, the CNI validates the performance of the methods ensuring proper operation and quality. The separate research projects, mainly from Psychology, Education, Business, Law, and other Social Sciences, will be covered by separate protocols.

b) State what the Investigator(s) hope to learn from the study. Include an assessment of the importance of this new knowledge.

This protocol will cover the development of new MR pulse sequences, reconstruction algorithms, data analysis methods and behavioral assays that will be shared with the CNI user community.

c) Explain why human subjects must be used for this project. (i.e. purpose of study is to test efficacy of investigational device in individuals with specific condition; purpose of study is to examine specific behavioral traits in humans in classroom or other environment)

The purpose of the study is to develop methods that can be applied for understanding the human brain. Brain structure and function can only be imaged and measured in living humans.

2. Study Procedures

a) Please SUMMARIZE the research procedures, screening through closeout, which the human subject will undergo. Refer to sections in the protocol attached in section 16, BUT do not copy the clinical protocol. Be clear on what is to be done for research and what is part of standard of care.

Adults ages 18-70 will participate in the proposed research.

Subjects will be screened prior to scanning to ensure that they are: not claustrophobic, not carrying metal in/on their body which can't be taken off for the scan, without a history of neurological, mental or cognitive impairment, and of normal hearing.

Also prior to scanning, participants will fill a screening form prepared by the center for Cognitive and Neurobiological Imaging (CNI) to ensure that there are no ferromagnetic materials on the subject. Participants will lie on a MR table within the magnet (field strength 3.0 Tesla) for up to 2 hours while the images are acquired. Participants may participate in more than one scanning session scheduled on separate days. Participants will wear earplugs and their heads will be held secure with foam padding to minimize movement. Under certain circumstances we may record the participants eye-movements using a specialized eye movement instrument compatible with the MRI scanner.

These videos are of one (1) eye of the participant only and do not include other facial features.

Images of the brain will be obtained in one or more of the

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

following conditions:

1. Participants are presented stimulus information (e.g., visual images/patterns, or movies, or sounds).
2. Participants may be required to make a response (e.g., push a button) regarding the stimuli.
3. Participants will be asked to lie still with no stimulation for anatomical imaging.

The presented stimuli will not contain any offensive content.

b) Explain how the above research procedures are the least risky that can be performed consistent with sound research design.

There are no known significant risks with the MR procedure.

Due to the rapid rate of change of magnetic field gradients that can be attained with this imaging system the possibility exists for peripheral nerve stimulation which would result in tingling sensations or twitching. Dizziness and nausea may occur if the head is moved rapidly within the bore of the magnet.

There is a risk of heating from the radiofrequency coils, the cables of the coils, the cables from response boxes and other accessories, and the cables from physiological monitoring devices. These risks will be minimized by following industry-standard MR procedures.

Risk versus benefit ratio. The risks from this study to the subject are minimal. There are no potential risks which would have any lasting effects for the subject.

The knowledge to be gained from this study justifies the use of human subjects.

This study will use 3 different MR scanners, a 3T Premier and a 3T MR750 at the Lucas Center, as well as a 3T Ultra-High Performance system at the CNI. The Premier and MR750 systems are FDA approved for diagnostic use. The 3T Ultra-High Performance system while using a common software and hardware architecture to GE's Premier system uses a higher-performance gradient coil and is not FDA approved for diagnostic use and is subject to the 21 CFR 812 investigational device (IDE) regulations as well as 21 CFR 50 and 56. As described in the attached letter (UHP 3T Safety Letter.doc) the system has been tested by GE according to UL606001-1 and also for compliance with IEC 60601-2-33 (ed 3.1) -- meeting limits and guidelines for peripheral nerve stimulation, patient thermal, SAR limit, acoustic noise, flammability rating UL94-5VA for safety covers, hydrostatic pressure, electrical hazards, dielectric strength and pinch point. The MRI scans in this study will also utilize operational parameters within FDA guidelines for Nonsignificant Risk thus an Investigational Device Exemption

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

(IDE) from FDA should not be necessary. The research conducted under this protocol is not to evaluate the safety or efficacy of this device.

In support of this research study, some of the image acquisition pulse sequences) and post-processing software will be developed in collaboration with GE Healthcare. Any such software will be considered investigational, will function as a non-significant risk device, and is subject to the 21 CFR 812 investigational device(IDE) regulations as well as 21 CFR 50 and 56. The investigational image acquisition software will conform to FDA guidelines for MR safety related to heating (SAR), peripheral nerve stimulation (dB/dt), and acoustic noise.

Please see the attached document "Information for IRBs" provided by GE Healthcare.

- c) **State if deception will be used. If so, provide the rationale and describe debriefing procedures. Since you will not be fully informing the participant in your consent process and form, complete an alteration of consent (in section 13). Submit a debriefing script (in section 16).**

No deception will be used.

- d) **State if audio or video recording will occur. Describe what will become of the recording after use, e.g., shown at scientific meetings, erased. Describe the final disposition of the recordings.**

Under certain circumstances we may record the participants' eye-movements using a specialized eye movement instrument compatible with the MRI scanner. These videos are of one (1) eye of the participant only and do not include other facial features. Any data that may be published in scientific journals or shown at scientific meetings will not reveal the identity of the subjects. All subjects are given an alphanumeric code and all data is stored on highly secure computer networks.

- e) **Describe alternative procedures or courses of treatment, if any, that might be advantageous to the participant. Describe potential risks and benefits associated with these. Any standard treatment that is being withheld must be disclosed in the consent process and form. (i.e. standard-of-care drug, different interventional procedure, no procedure or treatment, palliative care, other research studies).**

The study does not involve treatment.

- f) **Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?**

The study does not involve treatment.

- g) **Study Endpoint. What are the guidelines or end points by which you can evaluate the different treatments (i.e. study drug, device, procedure) during the study? If one proves to be clearly more effective than another (or others) during the course of a study, will the study be terminated before the projected total participant population has been enrolled? When will the study end if no important differences are detected?**

The study does not involve treatment.

3. Background

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

a) Describe past experimental and/or clinical findings leading to the formulation of the study.

Specifying the neural basis of thought and emotion can only be accomplished with advanced biomedical imaging techniques. Relatively little is known about the functional and structural anatomy of human brains - most relevant experimental research is an extrapolation from rodent and monkey studies. Until thirty years ago, only positron emission tomography (PET) and, to some extent, brain topographic mapping using EEGs, has yielded information about the human brain. PET, however, has several limitations. For example, PET (1) requires that subjects be exposed to radioactive substances, (2) has poor temporal and spatial resolution, and (3) requires averaging over subjects, so that one cannot obtain reliable information about individuals. EEG mapping provides good temporal information, on the order of tens of milliseconds, but is severely limited by the degree of spatial information it can provide.

Recent advances in magnetic resonance imaging (MRI) have allowed, for the first time, the opportunity to map and measure brain activity (functional MRI; fMRI) and to estimate the white matter and material properties of the living human brain.

Studies of function and structure have great potential for understanding the behaving human brain. These methods are quite safe because they do not require exposure to any radioactive substance, and can be implemented on MRI scanners present throughout much of the world.

The work under this protocol will lead to advances in MRI techniques for measuring both structure and function in the human brain. These developments will have an immediate impact on all of the users of the CNI, and we hope they will also have a long-term impact for other research sites studying the human brain.

b) Describe any animal experimentation and findings leading to the formulation of the study.

N/A

4. Radioisotopes or Radiation Machines

- a) List all standard of care procedures using ionizing radiation (radiation dose received by a subject that is considered part of their normal medical care). List all research procedures using ionizing radiation (procedures performed due to participation in this study that is not considered part of their normal medical care). List each potential procedure in the sequence that it would normally occur during the entire study. More Info**

Identify Week/Month of study	Name of Exam	Identify if SOC or Research
------------------------------	--------------	-----------------------------

- b) For research radioisotope projects, provide the following radiation-related information:**

Identify the radionuclide(s) and chemical form(s).

For the typical subject, provide the total number of times the radioisotope and activity will be administered (mCi) and the route of administration.

If not FDA approved provide dosimetry information and reference the source documents (package

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

insert, MIRD calculation, peer reviewed literature).

c) For research radiation machine projects, provide the following diagnostic procedures:

For well-established radiographic procedures describe the exam.

For the typical subject, identify the total number of times each will be performed on a single research subject.

For each radiographic procedure, provide the setup and technique sufficient to permit research subject dose modeling. The chief technologist can usually provide this information.

For radiographic procedures not well-established, provide FDA status of the machine, and information sufficient to permit research subject dose modeling.

d) For research radiation machine projects, provide the following therapeutic procedures:

For a well-established therapeutic procedure, identify the area treated, dose per fraction and number of fractions. State whether the therapeutic procedure is being performed as a normal part of clinical management for the research participants's medical condition or whether it is being performed because the research participant is participating in this project.

For a therapeutic procedure that is not well-established, provide FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions.

5. Devices

a) Please list in the table below all Investigational Devices (including Commercial Devices used off-label) to be used on participants.

5.1 Device Name : CNI 3T UHP

Describe the device to be used.

3T G.E. Healthcare wholebody MR system
This study is covered under the
GE/Stanford Psych
Research Contract Agreement

Manufacturer : GE

Risk : Non-significant

Y I confirm the above are true.

Rationale for the device being non-significant risk:

The GE 3T Ultra High Performance (UHP) MRI scanner is an upgrade of an FDA-approved 3T MR750 scanner but is not itself FDA approved.

The UHP scanner utilizes components from GE's 3T Signa Premier scanner (an FDA approved system) including gradient drivers, power supply, transmit and receive system, but uses a higher-performance gradient coil. The scanner has been tested by GE according to UL606001-1 and for compliance with IEC60601-2-33 (ed 3.1), meeting limits and guidelines for peripheral nerve stimulation, patient thermal, SAR limit, acoustic

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

noise, flammability rating UL94-5VA for safety covers, hydrostatic pressure, electrical hazards, dielectric strength and pinch point.

MRI research scans also frequently require specialized research software, but this will conform to FDA guidelines for MR safety related to heating (SAR), peripheral nerve stimulation (dB/dt), and acoustic noise.

As a result, the 3T UHP system is considered a non-significant risk investigational device and is subject to 21 CFR 812 investigational device (IDE) regulations as well as 21 CFR 50 and 56. The MRI scans in this study using the UHP scanner will utilize operational parameters within FDA guidelines for Nonsignificant Risk thus an Investigational Device Exemption (IDE) from FDA should not be necessary.

In addition to the GE receive coil components that are included with the UHP system, there are some non-GE coils. These devices are legally marketed components, used in accordance with their labelling, and are of non-significant risk. They include 32 channel and 16 channel receive-only brain RF coil arrays, manufactured by Nova Medical Inc, and an Invivo 8-channel coil.

Sponsor of Project

Indicate who is responsible for submitting safety reports to the FDA:

Y The sponsor is the STANFORD (SU, SHC, LPCH, VA) investigator.

Please read the following:

Sponsor-Investigator Research Requirements

If you would like further information on this process and/or assistance prior to submitting your protocol contact: The Stanford Center for Clinical and Translational Education and Research (Spectrum) at clinicaltrials@med.stanford.edu or for cancer research contact: ccto-regulatory@stanford.edu

Y I have read and understand the above guidance.

Ordering, Storage and Control

To prevent the device being used by a person other than the investigator, and in someone other than a research participant: Confirm that the device will be handled according to the SHC/LPCH policy for Investigational New Devices or as appropriate. If no, please provide an explanation. :

N Confirm?

The CNI is not part of either hospital, but we do restrict access to the scanner by keycard and require operators to achieve appropriate safety training.

5.2 Device Name : Lucas Center 3T MRI Systems

Describe the device to be used.

The Lucas Center GE 3T Systems

Manufacturer : GE

Risk : Non-significant

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

Y I confirm the above are true.

Rationale for the device being non-significant risk:

The Lucas Center facility includes two 3T MR scanners: one is a GE 3T MR750, the other is a GE 3T Premier system, both of which are FDA approved for diagnostic use. These will be the only MR systems at Lucas used for data acquisition. There are other MR systems at Lucas including a 3T PET/MR system and a 7T MR system but neither of these nor any other imaging system at Lucas will be used for this project.

The core MR imaging devices themselves are not investigational. The MR research being conducted requires highly specialized equipment and imaging software that does not exist in the clinical MR market so it is designed and implemented by researchers at the CNI and our collaborators.

Although some of the imaging software and equipment are not FDA approved, they have been tested for safety and are very similar to what is used regularly in clinical MR examinations. The MR personnel are highly trained in the set-up, utilization, and monitoring of this equipment.

In support of this research study, some of the image acquisition pulse sequences) and post-processing software will be developed in collaboration with GE Healthcare. Any such software will be considered investigational, will function as a non-significant risk device, and is subject to the 21 CFR 812 investigational device (IDE) regulations as well as 21 CFR 50 and 56. The investigational image acquisition software will conform to FDA guidelines for MR safety related to heating (SAR), peripheral nerve stimulation (dB/dt), and acoustic noise. Please see the attached document "Information for IRBs" provided by GE Healthcare.

Sponsor of Project

Indicate who is responsible for submitting safety reports to the FDA:

Y The sponsor is the STANFORD (SU, SHC, LPCH, VA) investigator.

Please read the following:

Sponsor-Investigator Research Requirements

If you would like further information on this process and/or assistance prior to submitting your protocol contact: The Stanford Center for Clinical and Translational Education and Research (Spectrum) at clinicaltrials@med.stanford.edu or for cancer research contact: ccto-regulatory@stanford.edu

Y I have read and understand the above guidance.

Ordering, Storage and Control

To prevent the device being used by a person other than the investigator, and in someone other than a research participant: Confirm that the device will be handled according to the SHC/LPCH policy for Investigational New Devices or as appropriate. If no, please provide an explanation. :

Y Confirm?

b) Please list in the table below all IDE Exempt Devices (Commercial Device used according to label,

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

Investigational In Vitro Device or Assay, or Consumer Preference/Modifications/Combinations of Approved Devices) to be used on participants.

6. Drugs, Reagents, or Chemicals

- a) Please list in the table below all investigational drugs, reagents or chemicals to be administered to participants.
- b) Please list in the table below all commercial drugs, reagents or chemicals to be administered to participants.

7. Medical Equipment for Human Subjects and Laboratory Animals

If medical equipment used for human patients/participants is also used on animals, describe such equipment and disinfection procedures.

There will be no animals (non-human) in the 3T scanner at CNI. The Lucas Center does conduct animal research on their 3T scanners, but the bed/table and accessories that are used for the animals is different than the table humans use. Physiologic monitoring equipment is cleaned with a commercial disinfectant such as Roccal, Conflick, Sani-Wipes, or a 10% Bleach solution. All RF coils and positioning accessories are wrapped in plastic wrap or plastic bags for use with animals. Everything, even if it is animal use only, is cleaned with the above disinfectants after every use even if they are wrapped in plastic. The Lucas Center is checked yearly by several groups at Stanford who approve animal research in human systems: Stanford Health & Safety. The Lucas Center is reviewed by: Stanford APLAC panel; USDA; NIH; and Aaalac.

8. Participant Population

- a) **State the following: (i) the number of participants expected to be enrolled at Stanford-affiliated site(s); (ii) the total number of participants expected to enroll at all sites; (iii) the type of participants (i.e. students, patients with certain cancer, patients with certain cardiac condition) and the reasons for using such participants.**

This research anticipates including 0-20 healthy volunteers per year. In many cases, the participants will be repeat studies of previously enrolled laboratory personnel in order to simply validate and confirm proper operation of MR sequences that have been updated to work on new MR scanner operating system releases. In other instances, new participants are enrolled in order to evaluate new MR methods we develop. There are no grant or study participant goals associated with this project--the purpose is to validate and improve MR sequences that are used by a number of other researchers conducting their studies at CNI. The participants will be recruited from the Stanford Psychology subject pool. Each participant may be scanned multiple times on separate days. This year, we enrolled only one new participant because many previously-enrolled participants agreed to be scanned again. The long-term target enrollment is 175 participants.

- b) **State the age range, gender, and ethnic background of the participant population being recruited.**

The participants will be adults of all genders and ethnicities.

- c) **State the number and rationale for involvement of potentially vulnerable subjects in the study (including children, pregnant women, economically and educationally disadvantaged, decisionally impaired, homeless people, employees and students). Specify the measures being taken to minimize the risks and the chance of harm to the potentially vulnerable subjects and the additional safeguards that**

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

have been included in the protocol to protect their rights and welfare.

About half of the volunteers are likely to be laboratory personnel, employees, and/or students. These individuals are often eager to participate in the research and we do not want to exclude them from participating. The Protocol Director will ensure that no laboratory personnel, employees, or students are coerced into participating and that all volunteers are made aware of their rights as research participants.

- d) If women, minorities, or children are not included, a clear compelling rationale must be provided (e.g., disease does not occur in children, drug or device would interfere with normal growth and development, etc.).**

N/A

- e) State the number, if any, of participants who are laboratory personnel, employees, and/or students. They should render the same written informed consent. If payment is allowed, they should also receive it. Please see Stanford University policy.**

About half of the volunteers are likely to be laboratory personnel, employees, and/or students. They will all render the same written informed consent as non-lab volunteers, following Stanford guidelines.

- f) State the number, if any, of participants who are healthy volunteers. Provide rationale for the inclusion of healthy volunteers in this study. Specify any risks to which participants may possibly be exposed. Specify the measures being taken to minimize the risks and the chance of harm to the volunteers and the additional safeguards that have been included in the protocol to protect their rights and welfare.**

All the participants will be healthy volunteers.

All subjects are first screened for health risks and determined to be free of ferromagnetic objects before entering the scanning room. Subjects are required to wear earplugs at all times during the scan to protect their ears from the noise of the scans. During a scan session, subjects may request to terminate the scan at any time through either the alarm button or microphones within the magnet.

- g) How will you identify and recruit potential participants about the research study? (E.g., by: chart review; notified by treating physician; response to ad). All final or revised recruitment materials, flyers, etc. must be submitted to the IRB for review and approval before use. You may not contact potential participants prior to IRB approval. See Advertisements: Appropriate Language for Recruitment Material.**

The potential participants will be recruited through the Stanford Psychology subject pool.

- h) Inclusion and Exclusion Criteria.**

Identify inclusion criteria.

We will include healthy volunteers.

Identify exclusion criteria.

Volunteers will be excluded for the usual contraindications to MRI exams, including pacemakers, surgical aneurysm clips, known metal fragments embedded in the body, including eyes. Women of childbearing age will not be included in this study if they might be pregnant. Subjects who are unable to attend to or respond to stimuli as required by the experimental protocol will also be excluded. Subjects with suspected cerebrovascular or pulmonary disease or a history of such will be excluded. Patients with a history of migraine, arterial hypertension, coronary heart disease, asthma, anemia, or epilepsy will also be excluded.

- i) Describe your screening procedures, including how qualifying laboratory values will be obtained. If you are collecting personal health information prior to enrollment (e.g., telephone screening), please request a waiver of authorization for recruitment (in section 15).**

Screening procedures are based on self report of the volunteer, questioning by the investigator, and a comprehensive screening form that will be administered prior to entrance to the scanner room.

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

- j) **Describe how you will be cognizant of other protocols in which participants might be enrolled. Please explain if participants will be enrolled in more than one study.**

Investigators will ask whether subjects are participating in more than one protocol.

- k) **Payment/reimbursement. Explain the amount and schedule of payment or reimbursement, if any, that will be paid for participation in the study. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of participants and that they do not constitute undue pressure on participants to volunteer for the research study. Include provisions for prorating payment. See payment considerations**

Volunteers will not be paid.

- l) **Costs. Please explain any costs that will be charged to the participant.**

There will be no cost to the participants.

- m) **Estimate the probable duration of the entire study. Also estimate the total time per participant for: (i) screening of participant; (ii) active participation in study; (iii) analysis of participant data.**

We anticipate continuing development and testing of MR methods for as long as the CNI service center is in operation, so there is no anticipated end date.

Estimated time per participant for (i) screening is less than one hour, (ii) active participation is 1 to 2 hours per scan session, and (iii) data analysis is several weeks. Participants will not be present during data analysis.

9. Risks

- a) For the following categories include a scientific estimate of the frequency, severity, and reversibility of potential risks. Wherever possible, include statistical incidence of complications and the mortality rate of proposed procedures. Where there has been insufficient time to accumulate significant data on risk, a statement to this effect should be included. (In describing these risks in the consent form to the participant it is helpful to use comparisons which are meaningful to persons unfamiliar with medical terminology.)

The risks of the Investigational devices.

There are no known significant risks with the MR procedure. Due to the rapid rate of change of magnetic field gradients that can be attained with this imaging system the possibility exists for peripheral nerve stimulation that would result in tingling or twitching. Dizziness and nausea may rarely occur if the head is moved rapidly within the bore of the magnet. There is a risk of heating from the radiofrequency coils, the cables of the coils, the cables from response boxes and other accessories, and the cables from physiological monitoring devices. Pads are placed between the subject and the sides of the magnet bore to reduce contact with heated elements and minimize this risk. Participants may terminate the scan at any time if discomfort occurs (or for any reason).

The risks of the Investigational drugs. Information about risks can often be found in the Investigator's brochure.

N/A

The risks of the Commercially available drugs, reagents or chemicals. Information about risks can often be found in the package insert.

N/A

The risks of the Procedures to be performed. Include all investigational, non-investigational and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).

N/A

The risks of the Radioisotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy) and

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

associated risks.

N/A

The risks of the Physical well-being.

There are no known significant risks with the MR procedure. Due to the rapid rate of change of magnetic field gradients that can be attained with this imaging system the possibility exists for peripheral nerve stimulation that would result in tingling or twitching. Dizziness and nausea rarely may occur if the head is moved rapidly within the bore of the magnet. There is a risk of heating from the radiofrequency coils, the cables of the coils, the cables from response boxes and other accessories, and the cables from physiological monitoring devices. Pads are placed between the subject and the sides of the magnet bore to reduce contact with heated elements to minimize this risk. Participants may terminate the scan at any time if discomfort occurs (or for any reason).

The risks of the Psychological well-being.

An MRI environment may be challenging for some adults, particularly those sensitive to closed environments (claustrophobia). We will inform participants about this problem, and be alert to any discomfort that the subjects may experience upon sliding in the scanner bore by oral communication. Subjects may stop the scan at any time using a hand held "squeeze ball".

The risks of the Economic well-being.

N/A

The risks of the Social well-being.

N/A

Overall evaluation of Risk.

Low - innocuous procedures such as phlebotomy, urine or stool collection, no therapeutic agent, or safe therapeutic agent such as the use of an FDA approved drug or device.

- b) If you are conducting international research, describe the qualifications/preparations that enable you to both estimate and minimize risks to participants. Provide an explanation as to why the research must be completed at this location and complete the [LINKFORINTERNATIONALRESEARCHFORM] International Research Form. If not applicable, enter N/A.**

N/A

- c) Describe the planned procedures for protecting against and minimizing all potential risks. Include the means for monitoring to detect hazards to the participant (and/or to a potential fetus if applicable). Include steps to minimize risks to the confidentiality of identifiable information.**

Pads are placed between the subject and the sides of the magnet bore to reduce contact with warm elements. Subjects may terminate the scan at any time if discomfort occurs (or for any other reason). Subject confidentiality is maintained through an alphanumeric coding system. All data are stored on a highly secure file server maintained by a professional systems administrator and physically secured behind two locked doors. Any copies of data that leave the physically secure zone (e.g., on a laptop) will be encrypted.

- d) Explain the point at which the experiment will terminate. If appropriate, include the standards for the termination of the participation of the individual participant Also discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the participants.**

An experiment will terminate upon the subject's request at any time. This request may be oral communication or through a squeeze ball held by the subject during the scans. The experimenter may stop the experiment if (s)he notices discomfort or suspects any subject discomfort.

- e) Data Safety and Monitoring Plan (DSMP). See guidance on Data Safety and Monitoring.**

A Data and Safety Monitoring Plan (DSMP) is required for studies that present Medium or High risk to participants. (See Overall Evaluation of Risk above). If Low Risk, a DSMP may not be necessary. Multi-site Phase III clinical trials funded by NIH require the DSM Plan to have a Data Safety Monitoring Board or Committee (DSMC or DSMB). The FDA recommends that all multi-site clinical

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

trials that involve interventions that have potential for greater than minimal risk to study participants also have a DSMB or DSMC.

The role of the DSMC or DSMB is to ensure the safety of participants by analyzing pooled data from all sites, and to oversee the validity and integrity of the data. Depending on the degree of risk and the complexity of the protocol, monitoring may be performed by an independent committee, a board (DSMC/DSMB), a sponsor's Data Safety Committee (DSC), a Medical Monitor, a sponsor's safety officer, or by the Protocol Director (PD).

Describe the following:

What type of data and/or events will be reviewed under the monitoring plan, e.g. adverse events, protocol deviations, aggregate data?

The MR and related physiological data will be captured and stored in a secure database server. The investigations under this work statement will use the information technology environment of the CNI. Data acquired from the MR instrument will be stored in the CNI instance of the Flywheel data management system. This is a HIPAA compliant system that is designed to steward MR data by recording important metadata and maintaining participant confidentiality.

Identify who will be responsible for Data and Safety Monitoring for this study, e.g. Stanford Cancer Institute DSMC, an independent monitoring committee, the sponsor, Stanford investigators independent of the study, the PD, or other person(s).

Protocol Director

Provide the scope and composition of the monitoring board, committee, or safety monitor, e.g., information about each member's relevant experience or area of expertise. If the Monitor is the Stanford Cancer Center DSMC or the PD, enter N/A.

N/A

Confirm that you will report Serious Adverse Events (SAEs), Suspected Unexpected Serious Adverse Reactions (SUSARs), or Unanticipated Problems (UPs) to the person or committee monitoring the study in accordance with Sponsor requirements and FDA regulations.

Should they arise, I will report any SAEs, SUSARs, and UPs in accordance with FDA requirements.

If applicable, how frequently will the Monitoring Committee meet? Will the Monitoring Committee provide written recommendations about continuing the study to the Sponsor and IRB?

N/A

Specify triggers or stopping rules that will dictate when the study will end, or when some action is required. If you specified this in Section 2g [Study Endpoints], earlier in this application enter 'See 2g'.

See 2g.

Indicate to whom the data and safety monitoring person, board, or committee will disseminate the outcome of the review(s), e.g., to the IRB, the study sponsor, the investigator, or other officials, as appropriate.

N/A

Select One:

- Y The Protocol Director will be the only monitoring entity for this study.
This protocol will utilize a board, committee, or safety monitor as identified in question #2 above.

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)

Approval Period: 04/22/2020 - 09/24/2020

10. Benefits

- a) Describe the potential benefit(s) to be gained by the participants or by the acquisition of important knowledge which may benefit future participants, etc.

None.

11. Privacy and Confidentiality

Privacy Protections

- a) Describe how the conditions under which interactions will occur are adequate to protect the privacy interests of participants (e.g., privacy of physical setting for interviews or data collection, protections for follow-up interactions such as telephone, email and mail communications).

Subjects will be contacted by the a member of the research team. The study will take place in the CNI, where numerous studies with healthy volunteers are conducted on a daily basis. The settings for data collection and temporary data storage in the CNI will be reviewed routinely. Subjects are provided with individual lockers for storing their personal belongings during the scan. Subjects may use a locked room for changing their clothes. The scanner suite is populated by the members of the research team only. Any additional guests in the scanner suite are approved by the experimenter and the subject. Consent forms will be reviewed and signed in an anteroom in the scanner suite. The room is part of the scanner suite, and hence it is locked and accessible only to members of the research team. Subjects will be given adequate time and space to sit down and comfortably and privately review the consent forms and screening forms.

Confidentiality Protections

- b) Specify PHI (Protected Health Information). PHI is health information linked to HIPAA identifiers (see above). List BOTH health information AND HIPAA identifiers. If you are using STARR, use the Data Privacy Attestation to ensure that your request will match your IRB-approved protocol. Be consistent with information entered in section 15a.

Some health information, such as previous surgeries and pregnancy status, is collected on a screening questionnaire that the subject completes at the beginning of the scanning session after they have signed the informed consent. However, this health information is not part of the research data collected, and is only used to ensure that it is safe for the subject to enter the MR scanner. The screening forms are archived in a locked drawer inside a locked office, which is in an access-controlled zone in the MR suite. Additional potentially identifiable data are collected within the scan session itself, in the form of the MRI brain images.

- c) You are required to comply with University Policy that states that ALL electronic devices: computers (laptops and desktops; OFFICE or HOME); smart phones; tablets; external hard disks, USB drives, etc. that may hold identifiable participant data will be password protected, backed up, and encrypted. See <http://med.stanford.edu/datasecurity/> for more information on the Data Security Policy and links to encrypt your devices.

Provide any additional information on ALL data security measures you are taking. You must use secure databases such as <https://researchcompliance.stanford.edu/panels/hs/redcap> RedCap. If you are unsure of the security of the system, check with your Department IT representative. Please see <http://med.stanford.edu/irt/security/> for more information on IRT Information Security Services and

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

http://www.stanford.edu/group/security/securecomputing/mobile_devices.html for more information for securing mobile computing devices. Additionally, any PHI data on paper must be secured in an locked environment.

By checking this box, You affirm the aforementioned. Y

Documents that can identify the participants will be kept in locked cabinets inside locked offices. Electronic data that can identify the participants will be stored on a secure server managed by a professional system administrator and housed in a physically secure location within the access-controlled MR suite. Access to these data will be limited to the research team and coordinators via secure password protection using the Stanford Kerberos system, and encrypted using protocols such as SSH and SSL. Any data that are stored outside of the physically secure zone will be stored only on encrypted devices. Subject names and other identifiable data will be removed prior to scientific presentations and publications.

- d) Describe how data or specimens will be labeled (e.g. name, medical record number, study number, linked coding system) or de-identified. If you are de-identifying data or specimens, who will be responsible for the de-identification? If x-rays or other digital images are used, explain how and by whom the images will be de-identified.**

The research team is responsible for de-identifying the data while sending it from the scanner and preprocessing it at the lab. Subjects' data are stored under a directory identified only by an alphanumeric code.

- e) Indicate who will have access to the data or specimens (e.g., research team, sponsors, consultants) and describe levels of access control (e.g., restricted access for certain persons or groups, access to linked data or specimens).**

Access to the data will be limited to the research team via secure password protection using encryption protocols such as SSH and SSL.

GE Scientists who are on-site for support of this study will not be exposed or have access to any protected health information; additionally, all data provided to GE Healthcare as part of this research will be de-identified.

- f) If data or specimens will be coded, describe the method in which they will be coded so that study participants' identities cannot be readily ascertained from the code.**

Confidentiality is strictly maintained through the use of alphanumeric codes.

Any data that may be published in scientific journals will be anonymized - no subject identities will be revealed. In the interest of public safety, subject information will be provided to Federal and regulatory agencies as required. The Food and Drug Administration, for example, has the right to inspect research records and, therefore, could learn subject identities if subjects are involved in any study performed under FDA supervision.

- g) If data or specimens will be coded, indicate who will maintain the key to the code and describe how it will be protected against unauthorized access.**

All subjects are given an alphanumeric code. The key to the code is maintained on the secure server and only accessible to research team members via secure password-protected methods using encryption.

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

- h) If you will be sharing data with others, describe how data will be transferred (e.g., courier, mail) or transmitted (e.g., file transfer software, file sharing, email). If transmitted via electronic networks, describe how you will secure the data while in transit. See <http://www.stanford.edu/group/security/securecomputing/> <http://www.stanford.edu/group/security/securecomputing/>. Additionally, if you will be using or sharing PHI see <https://uit.stanford.edu/security/hipaa> <https://uit.stanford.edu/security/hipaa>.

Only anonymized data will be shared with individuals outside of the research team. The investigations under this work statement will use the information technology environment of the CNI. Data acquired from the MR instruments will be stored in the CNI instance of the Flywheel data management system. This is a HIPAA compliant system that is designed to steward MR data by recording important metadata and maintaining data confidentiality. All access to the data will require secure login to the Flywheel system. All transfers of data will involve secure, encrypted protocols, such as SSL and SSH.

- i) How will you educate research staff to ensure they take appropriate measures to protect the privacy of participants and the confidentiality of data or specimens collected (e.g. conscious of oral and written communications, conducting insurance billing, and maintaining paper and electronic data)?

They will take the CITI training and the safety training at the CNI in which they will learn the importance of confidentiality of MR and related physiological data.

12. Potential Conflict of Interest

Investigators are required to disclose any financial interests that reasonably appear to be related to this protocol.

Financial Interest Tasks

Investigators	Role	Email	Has Financial Interest?	Date Financial Interest Answered	Date OPACS Disclosure Submitted	Date OPACS Review Completed
Brian A Wandell	PD	wandell@stanford.edu	N	09/06/2019		

13. Consent Background

13.1 Consent CNI Informed Consent

Check if VA related

- a) Describe the informed consent process. Include the following.
- Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)
 - When and where will consent be obtained?
 - How much time will be devoted to consent discussion?
 - Will these periods provide sufficient opportunity for the participant to consider whether or not to

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)

Approval Period: 04/22/2020 - 09/24/2020

participate and sign the written consent?

v) What steps are you taking to minimize the possibility of coercion and undue influence?

vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.

(i) A member of the research team will obtain consent from all study participants. (ii) The research team will also obtain written consent from the participants at the beginning of the imaging session at the CNI or the Lucas Center. (iii) Approximately 15 minutes for the written consent. (iv) Yes. (v) Participants will be given every opportunity to withdraw from the study and be made aware of their rights to minimize the possibility of coercion and undue influence. (vi) N/A.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See HRPP Chapter 12.2 for guidance.

The experimental procedure and informed consent will be discussed with the subject. The experimenter only asks the subject to sign the consent forms if the subject first indicates verbally that they understand the procedure and give their consent, and only after all questions the subject has have been answered. All participants of this study are native English speakers with no hearing impairments.

c) What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent, (iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

Only adult subjects competent to provide consent will be asked to participate. Competence is assessed through one-on-one discussion of the experimental procedure and the consent process prior to obtaining written consent.

14. Assent Background (less than 18 years of age)

15. HIPAA Background

16. Attachments

Attachment Name	Attached Date	Attached By	Submitted Date
CNI MR Screening Form	12/27/2010	bobd	
MR-Information for IRBs	01/18/2011	atsushi1	
Sona System Recruiting Text	01/24/2011	jhowden	
UHP 3T Safety Letter	01/21/2020	akerr	
UHP 3T Safety Letter Signed	01/22/2020	sfelice	

Obligations

The Protocol Director agrees to:

- Adhere to principles of sound scientific research designed to yield valid results

Title : Development and Evaluation of Functional and Quantitative MRI Techniques for Cognitive and Neurobiological Imaging (CNI)
Approval Period: 04/22/2020 - 09/24/2020

- Conduct the study according to the protocol approved by the IRB
- Be appropriately qualified to conduct the research and be trained in Human Research protection, ethical principles, regulations, policies and procedures
- Ensure all Stanford research personnel are adequately trained and supervised
- Ensure that the rights and welfare of participants are protected including privacy and confidentiality of data
- Ensure that, when de-identified materials are obtained for research purposes, no attempt will be made to re-identify them.
- Disclose to the appropriate entities any potential conflict of interest
- Report promptly any new information, modification, or unanticipated problems that raise risks to participants or others
- Apply relevant professional standards.

Any change in the research protocol must be submitted to the IRB for review prior to the implementation of such change. Any complications in participants or evidence of increase in the original estimate of risk should be reported at once to the IRB before continuing with the project. Inasmuch as the Institutional Review Board (IRB) includes faculty, staff, legal counsel, public members, and students, protocols should be written in language that can be understood by all Panel members. The investigators must inform the participants of any significant new knowledge obtained during the course of the research.

IRB approval of any project is for a maximum period of one year. For continuing projects and activities, it is the responsibility of the investigator(s) to resubmit the project to the IRB for review and re-approval prior to the end of the approval period. A Notice to Renew Protocol is sent to the Protocol Director 7 weeks prior to the expiration date of the protocol.

<https://stanfordmedicine.box.com/shared/static/qbsi8u8h47qsotxhdpuzz50xlrqao0sgo.pdf> Report promptly any new information, complaints, possibly serious and/or continuing noncompliance, or unanticipated problems involving risks to participants or others.

All data including signed consent form documents must be retained for a minimum of three years past the completion of the research. Additional requirements may be imposed by your funding agency, your department, or other entities. (Policy on Retention of and Access to Research Data, Research Policy Handbook,

<http://doresearch.stanford.edu/policies/research-policy-handbook/conduct-research/retention-and-access-research-data>)

APPROVAL LETTER/NOTICE NOTE: List all items (verbatim) that you want to be included in your approval letter (e.g., Amendment date, Investigator's Brochure version, consent form(s) version(s), advertisement name, etc.) in the box below.

Y By checking this box, I verify that I, as the Protocol Director (PD) responsible for this research protocol, have read and agree to abide by the above obligations, or that I have been delegated authority by the PD to certify that the PD has read and agrees to abide by the above obligations.