MRI and fMRI in Human Subjects Research

Guidance for FAU Faculty, Staff & Students

1 OVERVIEW

The evolution of MRI technology from clinical to academic settings raises questions about how to protect the safety of research participants without impeding important research. Several organizations, such as the National Institute of Mental Health (NIMH) and the American College of Radiology (ACR) have taken the lead in addressing this important issue. To ensure that MRI research at Florida Atlantic University meets the highest ethical and safety parameters, the FAU IRBs have provided this summary of the organizations' key recommendations. The goal of this document is to inform researchers about the unique safety concerns of using MRI in human subjects' research. This document is a guideline for writing protocols involving MRI or fMRI for researchers to submit for IRB review.

2 PREPARING THE IRB SUBMISSION

When preparing your IRB submission, please address the following points regarding MRI use and safety into your overall research protocol:

2.1 SCREENING: SINGLE MOST IMPORTANT SAFETY STEP

- In the Research Methods section of the IRB protocol, discuss the procedures for screening participants to determine if they meet inclusion and exclusion criteria for the MRI. (See Appendix 1 and 2) Inclusion and exclusion criteria should include conditions that are not compatible with having an MRI (i.e.: age, pregnancy, pacemakers, external fixation devices, cochlear implants etc.).
- Be explicit on the MRI contraindication for your protocol. Absolute contraindications to scanning may include: pregnancy, seizure disorder, infusion pumps, anxiety disorder, weight over 300 lbs.
- Explain in detail what steps are in place to screen for pregnancy and whether you intend to exclude pregnant participants. Specify if women of childbearing potential will undergo pregnancy testing prior MRI procedures. Specify time lines for the pregnancy test (i.e.: at screening time and/or at MRI time). **Note:** The method chosen may have potential privacy or legal implications. Consider the method that best

meets the needs of your target population. Remember to include specifics in the consent form (s) as applicable.

- Attach a copy of the screening form to be used (see Appendix 1) and discuss whether a screening interview will be used as a supplemental procedure. Specify how the screening process will be tailored to the participant's comprehension level and language requirements. (Appendix 2: Spanish screening form). Ideally, the screening tool should be written at a 6th grade reading level, even if participants have higher education levels.
- Alternatively, a third party should be present to help confirm that the participant satisfies the screening criteria for MRI safety.
- Discuss how concerns that arise from screening will be resolved.
- Those subjects with major contraindications [1] to MRI scanning should only be included if potential benefits have been appropriately weighed against the risks. A justification must be included in the IRB protocol.
- If screening reveals there are "minor" contraindications[2] to having an MRI, inform the participants about these risks during the consent process.
- Discuss any plans you may have for other, supplemental screening measures (e.g. those that may involve ionizing radiation) and discuss the risks and benefits.
- Discuss what measures you will have to ensure the effectiveness of your initial screening, i.e.: conducting a second screening, listing MR contraindications in the study recruitment material, having participants' empty pockets of metal objects, having participants remove all clothes and jewelry and wear a gown, or other methods.
- Explain if a hand-held high-strength magnet (e.g., ferromagnetic detector) is available, and whether it will be used as a primary or a supplemental screening measure.
- Clarify if repeat scans are planned with the participant. (e.g., daily or weekly for some period of time.) If so, discuss how you will screen for MRI risk factors prior to each scan.
- Describe how the investigators entering the scanning room will be scanned.

2.2 Emergency Procedures

- In the Risks section of the protocol, detail the staff members that will be available and their qualifications for dealing with emergencies (See section 2.8). At a minimum, at least two trained staff must be present at all times during which a participant/family member/companion is within an area of magnetic field risk. At least one of the two staff members must have Level II training.[3]

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[1] Major contraindications might include, but are not limited to, metal in the eyes, cardiac pacemakers, implanted cardioverter defibrillators, neurostimulation systems, and cochlear implants.

[2] A "minor" contraindication is one which is unlikely to pose a risk, but which may, if not carefully monitored, result in injury. (E.g., tattoo may be at minor risk for burns).

[3] Level II training: knowledge to protect the safety of others and to safely handle MRI related research equipment. Level II personnel are permitted to escort volunteers with the approval of the scanner operator.

- If the study protocol requires the use of contrast, please specify the procedure in detail as well as the risks of using IV contrast.
- For cases in which a MRI contrast agent is being administered via any route other than by mouth, a licensed physician must be on site and readily accessible to handle possible adverse reactions. The physician must be able to handle this issue as well as any additional emergencies not related to the MRI (e.g., sedation, cardiac issues, psychiatric issues, etc.) These details must be described in the IRB protocol.
- Specify the lines of authority for dealing with safety issues and whether the facility has a designated safety officer (DSO). Describe how study personnel will be informed about the DSO (e.g. standard operating procedures)
- Indicate whether the MRI facility has documented standard procedures (SOPs) for dealing with emergencies, including whom to call in the case of emergencies, how to remove a participant from the scanner and the scanning suite, when and how to quench the magnet, etc. [Attach a copy of those facility procedures or refer to a hyperlink.]
- If MRI scans will be conducted in nonmedical settings, specify in the informed consent form that emergency medical services may not be available onsite. This precaution is necessary to prevent participants from mistakenly interpreting the presence of the MRI scanner as evidence that they are in a medical setting with associated emergency medical services.
- Indicate if the MRI has established relationships with emergency resources in the community (hospitals, fire, police, etc.)
- Specify whether the MRI facility has a centralized process for reporting, managing and archiving incidents and adverse events associated with scanning. Discuss how any unanticipated problems involving risks to others will also be reported to the IRB. (See adverse events below)

2.3 Data Confidentiality & Privacy

- Since personal images (some with incidental findings) and screening tools (with sensitive medical information) will be collected, specify in the **Research Materials, Records, and Privacy** section of the protocol what will be done to protect participants' privacy and confidentiality. Will a coding system be used? What types of password protection and encryption will be used for electronic data? If research documents will be physically stored in paper form, how will they be secured and how will they be destroyed once no longer needed?
- If the images are being obtained by a facility that must abide by HIPAA regulations, include the standard HIPAA authorization form with your IRB submission.

2.4 Incidental Findings

Incidental findings are medical findings a researcher may discover while looking for something else related to the research. While it is not the intent of the researcher to diagnose a medical condition, any researcher using MRI for research purposes should be able to estimate the expected rate of incidental findings in his/her research, and plan

how this will be handled. Additionally the subjects must be informed of these procedures.

- In the **Research Materials, Records, and Privacy** section of the protocol, provide an expected incidental finding rate, based on comparable literature, and discuss how many findings you expect to be clinically significant. The researcher must outline the procedure that will be put in place for dealing with incidental findings. For instance, if the PI is not a clinical professional, or does not have an M.D. as an investigator on the study, he/she must include how incidental findings will be addressed as part of the study procedures. (See Informed Consent Section – Incidental Findings)
- MRI research protocol and consent form must include attestation of the research subject's preference as to whether or not he/she agrees to receive results of incidental findings.

2.5 Informed Consent For a Research MRI

If the protocol requires an MRI as part of other research procedures, tests, questionnaires or any other specific research activities, a separate consent form for the MRI should be included. If the main procedure of the study is the MRI, just one consent form will be required (See FAU Consent to participate in a Magnetic Resonance Imaging (MRI) Research Study)

In addition to the general requirements of a consent form[4], the following must be included when MRI scans are involved:

a) Whether participants will need to undergo regular pregnancy testing or provide date of last menstrual cycle;

b) The procedures, time commitment, and risk involved in repeat scanning;

c) A discussion of incidental findings, how they will be handled, and the possibility that this may lead to false positives, unnecessary worry, expense for medical follow-up, and possibly unpleasant or invasive medical tests. (Note: Despite the fact that the scan may not be of clinical caliber and/or that there may be no clinically trained investigators involved in the research, NIMH guidelines emphasize the importance of informing participants about the possibility that an abnormality may be detected or suspected in the process of the research, even if the clinical significance is not clear);

d) A statement in the procedures section that clearly distinguishes research scans from clinical scans, and emphasizes (if applicable) that the MRI facility is not a medical facility.

e) If research involves health information[5] , including mental or behavioral health, about living or deceased persons that will be (or was) obtained as part of a health care service please refer to the Guidance on HIPAA and research for additional considerations that must be addressed http://www.fau.edu/research/research-integrity/hipaa-and-research.php.

[4] FAU IRBNet Library Documents (Consent Templates). Researcher must have an active IRBNet account to access these documents.

[5] Assessment Tool 2: Am I Using Protected Health Information? (PHI). http://www.fau.edu/research/research-integrity/files/Assessment_Tool_2__Am_I_Using_Protected_Health_Information.pdf

2.6 RECRUITMENT

In the research proposal, (Section D - recruitment plan) in addition to inclusion/exclusion criteria for the overall study, list any conditions that would disqualify someone from having an MRI scan on relevant recruitment material such as ads, email text, etc. Inform the participant of the time commitment involved, especially if repeat scans are planned (e.g., volunteers will receive 3 MRI head scans, one per month, over 3 months).

2.7 TRAINING

- In the Resources section of the protocol, indicate whether the MRI facility has documented training procedures (certification, apprenticeship, written material) in place to help ensure participant safety.
- Research personnel should be trained on all elements relevant to their research practices. It is important to note that while a researcher or research coordinator (RC) can be present to give study requirements to the MRI technician, screen participants, and administer study-related interventions (stimuli, etc.), imaging of patient must be done by a qualified technician. Ultimately, the principal investigator (PI) and the designated safety officer (DSO) are responsible for ensuring that all involved have the appropriate training to protect the safety of study participants. Include certifications of training level I or level II as part of your IRB submission.

2.8 SAFETY

- In the Risks section of the protocol, specify (and attach documentation) on the MRI facilities safety procedures.
- If screening reveals that potential participants have implants or devices that are new or that have no safety data, researchers should consult the DSO and/or review sources such as www.MRIsafety.com to assess the compatibility of the devices with the MRI scanner's field. If information is unavailable, exclude the participant from study for safety reasons. www.MRIsafety.com is the official site of the Institute for Magnetic Resonance Safety, Education, and Research**.**
- In the risk section of the protocol, specify how those persons accompanying the participants will be scanned when entering the MRI environments (e.g. participant companion, parent of the child, etc.) (See Appendix 3).
- *If applicable*, discuss in the same section how the PI will assess the safety and compatibility of ***external*** research devices being brought into the MRI suite (such as non-FDA-approved devices developed for research, or devices for displaying stimuli or recording behavioral responses from the participant.) Provide a description of these devices and procedures for evaluating their safety; indicate what technical consultants (e.g., a biomedical engineer) have evaluated the safety of these devices in terms of magnet exposure, burn, and fire risk. (See section C4, NIMH Guidelines, for technical consultant criteria.)

2.9 Vulnerable Populations:

- In the Informed Consent Process section of the protocol, discuss what additional safeguards will be put in place for vulnerable populations, such as children, cognitively impaired, etc.
- Researchers conducting studies involving children as research participants should be proactive in obtaining permission during the informed consent process to inform the child's primary care physician of any incidental findings since parents may not fully appreciate the need for follow up.
- Researchers are also advised to have a plan for how to handle and report suspected child abuse or neglect, since a neuroimaging (fMRI) study may yield findings suggestive of abuse. Any proposed study to scan pediatric subjects should also address the special risks of high field magnets. Additionally, researchers should be sensitive to, and screen for, the presence of dental braces and retainers frequently worn by adolescents and to what extent these pose a safety issue (e.g., heating) or research issue (introducing artifacts in brain images of interest. Additional detail is available in section F of the NIMH guidelines.

2.10 Adverse Event Reporting:

In the Risks section of the protocol, discuss how unanticipated problems involving risk to subjects or others will be handled and reported. Under the Common Rule (45 CFR Part 46, Subpart A), an IRB must require reporting of all unanticipated problems resulting in risks to participants or others, even if there is no actual injury, as these hold implications for safety. In addition to reporting to the IRB, the PI and/or the MRI facility may be required to report adverse events to other regulatory or safety agencies.

3 Experimental Devices

Per section F6 of the NIMH guidelines, it is important to be aware if the research involves the study of an "experimental, non FDA approved medical device or ancillary devices designed to present stimuli and record responses in fMRI research." If applicable, also note whether improvements to the MRI machine itself are being studied. Indicate in section Research Methods of the IRB protocol what FDA review process has occurred or will occur. Review the FAU IRB policy on investigational devices and the IRB's investigational device exemption (IDE) checklist.