



LCNI Magnetic Resonance Imaging (MRI): Standardized Operating Procedures

Provided by Dr. Alison Burggren, Director of the Lewis Center for Neuroimaging
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These standard operating procedures will be used by all projects conducted at LCNI. Researchers wishing to deviate from these procedures must specify alternate procedures and explain all deviations from these SOPs in their IRB application, which must be submitted to LCNI before being submitted to the IRB with the understanding that this will lead to full UO IRB committee review of their study. New investigators will submit IRB materials to LCNI before IRB. Ongoing studies will incorporate these SOPs and text during their next amendment or continuing review.

Screening

All participants will be pre-screened by investigators using the LCNI screening form in order to reduce the number of participants excluded at the time of scanning. This form may be administered either as a self-report form or by an experimenter. It will be kept by LCNI.

An LCNI approved MRI technician (see below for training summary) will thoroughly screen all participants again ahead of each scanning session, using the same screening form, but conducted as a structured interview. Screening and consent is done in private. Parents/guardians will initially help with screening questions but, minors will also have the opportunity to ask confidential questions about safety and exclusions to the MRI technician without a parent/guardian present. The group of items that are standard exclusions (e.g. pacemaker, potential pregnancy) will not be individually interrogated, but asked as a group (i.e. "If any of these apply to you, please let the technician know you do not qualify").

Unremovable piercings are those that cannot be removed by the participants themselves prior to or at the lab. If participants are asked to remove unremovable piercings for the research prior to coming to LCNI, that is something that should be covered during the pre-screening process conducted by the investigators before they arrive at LCNI. LCNI will not be able to assist in the removal of any unremovable piercings and individuals who are unable or unwilling to remove piercings upon arrival to LCNI will not be able to receive a scan. Per the IRB, any risks, discomforts or costs associated with the removal of unremovable piercings being removed for research purposes should be described within the pre-screening and potential participants should know enough information about the research activities at time of pre-screening so they can make an informed decision about whether they want their unremovable piercings removed before they arrive in LCNI. Many items may be safe if we can properly identify them (e.g. pins in the knee from prior surgery). Any surgeries will be followed up on individually to the point where we can identify if there was anything inserted. When needed, we will consult Frank Shellock's book on MR compatible devices [Shellock, ISBN-13: 978-0989163217], the gold-standard for testing medical devices in MRI. If an individual reports having a device/implant/etc. that cannot be identified (or that would not be safe in the MRI), that individual will not be permitted in the scanner.

LCNI has two metal detectors (wand and wall-mounted unit), as well as small magnets to use if the technician deems it necessary, to test whether participants are free of potentially harmful metal before starting their scan. (Small magnets are used to test permanent retainers and other dental fixtures.)

The LCNI screening process is designed to ensure we have adequate knowledge about the individual to make an informed decision on whether or not it is safe to proceed with scanning at our center. The decision of whether or not to allow individuals to participate if they have elements in their bodies that do not pose a safety risk but may affect the clarity of the MRI scans, will be left to the investigator, who may consult with LCNI staff.

Participants will only be allowed to continue with the scanning procedures if the LCNI approved technician who conducts the pre-scan screening determines that it is safe for the individual to be scanned.

Consent

The consent process is done in private at LCNI. LCNI will not provide a separate consent form for scanning. Instead we provide standardized language that all protocols conducted at the LCNI must use unless they receive prior approval from the LCNI and IRB. The language attached in appendix A&B is provided to investigators to put in their consent forms. The consent form language not pertaining to MRI is not part of the standardized procedures here and will be reviewed by IRB using regular procedures.

Mock/Practice Procedure

All participants will be offered a practice session in our 'mock' scanner: a duplicate environment without the strong magnetic field. We strongly encourage all investigators to plan to 'mock' scan every minor. This practice environment allows LCNI staff and/or



investigators to pre-test and prepare participants for the real environment and to provide demonstration of details about the procedure.

Scanning Procedure

Before MR scanning, participants must empty their pockets and do a final check for metal. Depending on what they are wearing, the participants may be asked to remove their clothes and put on 'scrubs' (e.g. if they are wearing a shirt with metal buttons). They then walk into the MRI room, directly adjacent to the MR control room, accompanied by a technician that is approved by the LCNI director. Technicians will be approved based on their prior experience, at least 40hrs of initial training/experience, and a record of conducting at least 40 additional training/ supervision scans by LCNI Director, Chief Safety Officer, or Chief Physicist. Faculty members trained at other institutions will also be allowed to run the system once they have been supervised for 3 independent sessions. Operator Training will not be delegated to other trained members – all supervision will be done by LCNI staff (Director, Safety Officer, Physicist). Researchers will be required to be safety trained according to LCNI policy, which includes initial certification and yearly renewals (quiz and/or educational content) approved by the Director and/or Chief Safety Officer.

All participants will be given hearing protection in the form of earplugs and/or headphones as the MR scanner emits loud sounds during scanning. Participants will be placed on the bed and made comfortable with blankets and pillows in order to ensure that they can comfortably stay as still as possible. The participants will be given an emergency squeeze ball and instructed in its use. If the participant squeezes this ball at any time, the scanning will be stopped and the participant can be removed from the scanner if they wish.

Depending on the study, participants may be given additional equipment. All equipment used during the scanning must have been previously tested for MR-compatibility by LCNI staff. See details below for currently approved options.

Once the participant is prepared, the bed of the magnet moves the body part to be imaged to the center of the machine. For head studies, this typically means that half of an adult participant is within the magnet. For children, this means that a greater proportion of the body will be inside the magnet. For studies of lower extremities, participants go in feet first, and their chest and head are outside the machine on the bed. The staff ensures that the participant is comfortable, and then leaves the magnet room.

Staff operate from the MR control room. They have direct views of the participant and a communication system to talk to the participant, typically between each scan. They also have the squeeze ball alarm system for emergency notification during scans.

Multiple digital images or 'series' are taken, which focus on different types of tissue (fat, muscle, brain or water). These series last between ten seconds and ten minutes each, depending on what type of image is needed. The staff will routinely check with the participant and inform him/her of the type of series to be run next and the time it will take.

After all series have been run, the staff return to the MR room to extract the participant from the scanner and MR room environment. Informal questions by Investigator or LCNI staff make sure the participant is not light-headed/groggy before they get up from the bed and to make sure they are not in an anxious state before leaving the facility.

Risks Associated with MRI

Given the physics of MRI, there are three potential pathways for risk associated with MRI scanning: heating, sound, and static field itself.

The static magnetic field of the scanner presents the most significant risk if ferromagnetic objects are brought into the room. There is a risk these objects may be strongly attracted to the MRI machine. They may also lead to heating and burns. This can occur if the participant or LCNI equipment are not positioned properly inside the scanner by creating conductive loops.

To minimize this risk, LCNI-trained staff will conduct a thorough screening for any potential problems (research staff usually do this once before they arrive and LCNI does it again right before the scanning session), to make sure we have accounted for all MRI-related concerns. Participants who do not pass screening are not run. LCNI has a very conservative approach to screening, whereby any uncertainty by staff or participants about the veracity and completeness of the screening leads to cancellation of the scan. Participants are very carefully positioned in the magnet with special insulating pads to ensure no conductive loops are present.

The MRI scanner makes loud thumping, pounding and whining sounds during scans, which reaches levels that could cause hearing damage. Thus every person in the magnet room during scanning must wear hearing protection (earplugs and/or special headphones).

Some people become anxious and/or tired and/or claustrophobic from lying in the MRI machine. LCNI offers 'practice' sessions in a mock-scanner before the session to everyone and encourage their use, especially in people who do not know whether they are claustrophobic or not.

All participants are told that they may ask to stop the practice or real MRI scans at any time. They are given an emergency squeeze ball during the real MRI and instructed in its use. They may squeeze this ball at any time to stop the scan and be removed from the scanner.



Although there are no known risks to having an MRI during pregnancy, it is a time when the heart and brain are still developing and is listed as a reason for exclusion on our screening form. LCNI strongly encourages anyone who may be pregnant to wait until their pregnancy is finished to participate in research. See below for further policy on pregnancy.

No Clinical Interpretation

As noted in the consent form, although MRI is approved as a clinical device, LCNI does not have all scans read clinically. The consent form documents our procedures for incidental findings. LCNI staff are not qualified to provide a clinical opinion and thus cannot say whether something is abnormal or an anomaly; only a radiologist can determine that.

If the MR operator observes something in an image that he/she deems unexpectedly odd, the operator will immediately call this observation to the attention of the LCNI Director. The LCNI Director and MR safety officer will review the image. We will reach a consensus decision as to whether to seek a qualified clinical opinion. Participants that report having prior surgery or other structural abnormalities and have had prior MRIs, will not be sent for review. These expected abnormalities are beyond the scope of our expertise.

Images will be shared anonymously with a radiologist. The radiologist will inform the LCNI Director as to whether the participants should be told to follow-up with their doctor. If so, the director or the PI of the project will inform the participants of the recommendation of the radiologist. The participants will be told that they can take any scans to their doctors if they wish.

Pregnancy

LCNI policy is to properly and fully inform participants of current best practices and to strongly encourage that participants use an abundance of caution and choose to exclude themselves if they are or may be pregnant (see consent form). For almost all research studies, this will not adversely affect the research. Please see Appendix C for full text of IRB/LCNI subcommittee on MRI and pregnancy.

Research projects may have one of several standard options:

Coils

LCNI Siemens scanner is equipped with an array of coils to better investigate different parts of the brain/body. The most frequently used is the head coil, which looks like a helmet, and is designed to maximize quality in brain series. There are also coils for body, knee, shoulder, and other elements.

Sometimes, investigators require a different coil to complete the scope of the requested research. Fabrication of new coils will be performed either by the UO Machine Shop or by LCNI employees trained at the shop. Assembly of electronic components will be performed either by the UO Electronics Shop or by LCNI employees. Plans and schematics for coils will be based on standard designs in the scientific literature. Custom-built coils will meet the specifications for customer coils in Siemens' coil interface documentation as determined by the LCNI Physicist in consultation with Siemens. Additionally, the specific absorption rate for transmit coils will be characterized using the "Calorimetry Method" in NEMA Publication MS 8-1993, "Characterization of the Specific Absorption Rate for Magnetic Resonance Imaging Systems." All new coils will be tested extensively without human subjects present by LCNI staff and receive a green dot in order to document safety. If hardware with a green dot is removed from the scanner room, the green dot will be removed and it will need to be re-tested before being put back into use.

Physiological Monitoring

All devices deemed safe will have a green dot affixed to document safety testing in the MR environment. Projects may wish to collect additional information during MR-scanning, including heart rate, respiration rate, galvanic skin response, and pulse-oximetry. LCNI has MR-compatible devices to allow this monitoring. All devices that enter the MR room are tested ahead of time by LCNI staff without human subjects present to assess their safety. In most cases, these are owned, stored, and maintained by LCNI. If devices are removed from the LCNI, they must be retested for safety by LCNI staff, without human subjects present. If hardware with a green dot is removed from the scanner room, the green dot will be removed and it will need to be re-tested before being put back into use.

Behavioral Tests

Participants may be given equipment to provide visual, auditory, tactile, and/or other sensory stimuli. They may have additional equipment to allow them to respond to behavioral test conditions. Stimulus presenting equipment may include 'goggles' or screens that allow presentation via projector. Response equipment may include button boxes, pads, keys, or joysticks. As above, it is center policy that these devices are tested ahead of time; are typically owned, stored, and maintained by LCNI; and will get a green dot to document safety. If hardware with a green dot is removed from the scanner room, the green dot will be removed and it will need to be re-tested before being put back into use.



UNIVERSITY OF OREGON

LCNI SOP'S, Nov 2023



Appendix A: Adult Consent Text

Below please find the information needed for submitting an application to use LCNI in Human Subjects Research. Copy the text below into appropriate places in your consent document(s). Please review the LCNI standard operating procedures to see if your project will require any deviations from those procedures, if so please contact LCNI for approval first. State in your research plan that you will follow LCNI SOPs. Do not describe MRI procedures in your research plan. Finally, attach the latest LCNI metal screening form to your application when you submit it. All new investigators to the center will be required to submit their IRB packet to LCNI before sending it to the IRB. Any proposed changes to language or procedures must be discussed with LCNI ahead of time. These will go to full UO IRB.

LCNI Approved IRB CONSENT language

A. Intro [Please add the following paragraphs to your intro section leave in italics for review]:

This study uses the standard procedures for the Siemens Skyra or Prisma 3 Tesla MRI at the Lewis Center for Neuroimaging (LCNI). Magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) are approved by the US Food and Drug Administration (FDA) to look at structure and function of your brain and body. MRI uses a very strong magnetic field and radio frequency pulses to create digital pictures. There is no ionizing radiation (like X-rays) or injections into your body with this MRI.

Scans are done for research purposes only and cannot rule-out or confirm a diagnosis. A medical doctor does not always review the scans. However, if a member of the LCNI staff observes something unexpected in a scan, the scan will be sent anonymously to a radiologist. If the radiologist suggests that you follow-up with your regular doctor, we will discuss what the radiologist said in detail with you. You will be able to take all your images from this study to your doctor and the LCNI director can point out the area of possible concern, if needed.

B. Confidentiality [Please add the following sentences to your section on confidentiality leave in italics for review]:

Imaging data are kept on a secure computer by the LCNI with an anonymous code. There is no identifying information kept with LCNI imaging data. Access and information related to these data are described further in this section.

C. Risks [Please add the following sentences to your section on risks leave in italics for review]:

LCNI has multiple safety features to reduce the potential for harm. The strong magnetic field of the scanner presents a risk if some types of metallic magnetic objects are brought into the room. There is a risk these objects may be attracted to the MRI machine or they may lead to heating and burns to you. This can also occur if your body or our equipment are not positioned properly inside the scanner. There are safety rules to protect you from being hurt while in the MRI machine. We will ask you questions about any metal you may have on you or in you. This is to make sure you are not hurt. Depending on what you are wearing (like a shirt with metal buttons or pants with metal zipper), you may be asked to go into the bathroom and change some clothing and put on 'scrubs'. If you have metal on your body, such as rings, earrings, or other piercing, you will be asked to remove it. If you can not remove the metal, you will not be allowed to continue in the study. We will minimize this risk by carefully positioning you with special insulating pads. LCNI staff will conduct a thorough screening for any potential problems, to make sure we have accounted for all MRI-related concerns. Depending on what you are wearing (e.g. metal buttons or clasps), you may be asked to remove some clothing and put on 'scrubs'.

The MRI scanner makes loud thumping, pounding and whining sounds during scans, which may be discomforting to some people. You will be provided with hearing protection to reduce the noise from the scanner. You may become anxious and/or tired from lying in the MRI machine. Some individuals who are claustrophobic (scared of small spaces) may find the scanner too confining. To get an idea of what the experience of being scanned will be like, you may ask to do a 'practice' session in our mock-scanner before your session. You may ask to stop the practice or real MRI scans at any time. You will be given an emergency squeeze ball during the real MRI and instructed in its use. You may squeeze this ball at any time to stop the scan and be removed from the scanner.



Although there are no known risks to having an MRI when you are pregnant, it is a time when the heart and brain are still developing. Therefore if you think that you may be pregnant, we will encourage you to choose not to participate until you are finished with your pregnancy.

LCNI SOP'S, Nov 2023

Appendix B: Assent Text If you are studying minors use this LCNI Approved IRB PARENT and ASSENT language

Below please find the information needed for submitting an application to use LCNI in Human Subjects Research. Copy the text below into appropriate places in your consent document(s). Please review the LCNI standard operating procedures to see if your project will require any deviations from those procedures, if so please contact LCNI for approval first. State in your research plan that you will follow LCNI SOPs. Do not describe MRI procedures in your research plan. Attach the SOPs to your IRB application. Finally, attach the latest LCNI metal screening form to your application when you submit it. All new investigators to the center will be required to submit their IRB packet to LCNI before sending it to the IRB. Any proposed changes to language or procedures must be discussed with LCNI ahead of time. These will go to full IRB.

PARENT/GUARDIAN CONSENT:

- D. Intro [Please add the following paragraphs to your intro section leave in italics for review]:

This study uses the standard procedures for the Siemens Skyra or Prisma 3 Tesla MRI at the Lewis Center for Neuroimaging (LCNI). Magnetic resonance imaging (MRI) and magnetic resonance spectroscopy (MRS) are approved by the US Food and Drug Administration (FDA) to look at structure and function of your child's brain and body. MRI uses a very strong magnetic field and radio frequency pulses to create digital pictures. There is no ionizing radiation (like X-rays) or injections into your child's body with this MRI.

Scans are done for research purposes only and cannot rule-out or confirm a diagnosis. A medical doctor does not always review the scans. However, if a member of the LCNI staff observes something unexpected in a scan, the scan will be sent anonymously to a radiologist. If the radiologist suggests that your child may need to follow-up with your regular doctor, we will discuss what the radiologist said in detail with you. You will be able to take all the images of your child from this study to your doctor and the LCNI director can point out the area of possible concern, if needed.

- E. Confidentiality [Please add the following sentences to your section on confidentiality leave in italics for review]:

Imaging data are kept on a secure computer by the LCNI with an anonymous code. There is no identifying information kept with LCNI imaging data. Access and information related to these data are described further in this section.

- F. Risks [Please add the following sentences to your section on risks leave in italics for review]:

LCNI has multiple safety features to reduce the potential for harm to your child. The strong magnetic field of the scanner presents a risk if some types of metallic magnetic objects are brought into the room. There is a risk these objects may be attracted to the MRI machine or they may lead to heating and burns to your child. This can also occur if your child's body or our equipment are not positioned properly inside the scanner. We will minimize this risk by carefully positioning your child with special insulating pads. LCNI staff will conduct a thorough screening for any potential problems, to make sure we have accounted for all MRI-related concerns. Depending on what your child is wearing (e.g. metal buttons or clasps), your child may be asked to remove some clothing and put on 'scrubs'.

The MRI scanner makes loud thumping, pounding and whining sounds during scans, which may be discomforting to some people. Your child will be provided with hearing protection to reduce the noise from the scanner. Your child may become anxious and/or tired from lying in the MRI machine. Some individuals who are claustrophobic (scared of small spaces) may find the scanner too confining. To get an idea of what the experience of being scanned will be like, you or your child may ask to do a 'practice' session in our mock-scanner before your session. You or your child may ask to stop the practice or real MRI scans at any time. Your child will be given an emergency squeeze ball during the real MRI and instructed in its use. Your child may squeeze this ball at any time to stop the scan and be removed from the scanner.

If studying vulnerable females of childbearing age add the following to the PARENT/GUARDIAN documents:

Although there are no known risks to having an MRI when one is pregnant, it is a time when the heart and brain are still developing. Therefore if you think that your child may be pregnant, we will encourage you to choose not to have your child participate until they are finished with their pregnancy.



Assent for Research Participation (ages 7 – 11)

Template Assent Ages 7-11 may be found at irb.rap.uoregon.edu under the IRB > Library tab > Templates

[Please add the following text to your document]:

Today we are asking you to be in a research study. You can say yes or no. It is your choice. First, we will tell you about the study. Then we will ask if you want to be in it. You can ask any questions you want. We will also be talking to your parents or caregivers about the study. Even if your parents or caregivers say that it is okay for you to be in this study, you can still choose not to take part.

What is a research study?

A research study is a way people can learn things. We are trying to learn about how your brain and body work when you are asked to do things.

What will you do?

Describe all the research procedures using simple terms. If any parts of the study are experimental, explain those parts. Explain any medical terms or complex topics.

If you say yes to being in this study, you will do a few activities. These include:

- Answering questions about [insert type of questions]
- Playing some computer games
- Doing some activities about words and sounds, kind of like what you do in school
- Having a small amount of blood will be taken from your [insert location of blood draw like arm or finger if blood sample will be taken].

These activities will be done [describe where the research will take place if there is an additional location to LCNI and] at the Lewis Center for Neuroimaging on the UO campus.

- This study is being done at the Lewis Center for Neuroimaging on the UO campus. We want to take pictures of the inside of your body and brain using a big magnet. This magnet allows us to take pictures of how your brain and body work when you are doing activities. To take these pictures, you will lie down on a bed with the magnet around you. You may hear it called an MRI. You need to stay very still while we take the pictures. We will ask you lots of questions about metal to make sure you do not get hurt. If your clothes have metal on them, like a shirt with metal buttons, you will be asked to go into the bathroom and change your clothes and put on 'scrubs'.
- We will ask you to do a 'practice' session in our 'pretend' magnet that looks and sounds just like the 'real' magnet. We will do this before the real session to see if you want to do this study.

How long will it take?

We will see you [insert number of study sessions/visits]. Each time we see you, the visit will take about [insert hours or minutes]. We can take breaks if you get tired. Just ask us for a break.

Could anything bad happen?

Sometimes people feel tired or bored. If that happens, let us know and we will take breaks.

[Insert if blood draw is part of protocol] The stick from the needle to draw your blood may hurt a little, but the hurt will go away after awhile.



If you feel sick or are in pain when you do the activities, please tell your parent or caregiver and us.

If you are in the study, we will keep your answers private and not tell anyone. Sometimes people see or hear the answers that they should not see or hear. We will try very hard to make sure no one sees or hears your answers who should not.

Only the researchers and others with special permission will see your pictures. The pictures will be stored so your name is not on them. If anyone else sees the pictures, they will not know the pictures are of you.

MRI:

- To make sure you are safe, no metal objects like paper clips or metal buttons can be brought into the magnet room where the pictures will be taken. Metal objects may cause heating or burn you. If you have metal on your body, such as rings, earrings, or other piercing, you will be asked to remove it. If you can not remove the metal, you will not be allowed to continue in the study.
- We will help you get in the magnet and place special pads around you. The pads help to keep you safe.
- The magnet makes loud thumping, pounding and whining sounds during scans. These sounds may be loud and annoying. You will wear headphones and/or earplugs during the scan to protect your ears.
- You may be nervous and/or tired by lying in the magnet machine. Some people are scared of small or enclosed places and may not like the magnet. If you want to get out you can tell us.

Could being in this study help you or others?

Usually, kids have fun in our study, and being in our study will help us to learn more about [reiterate purpose].

We do not know if this study will help you. We may learn something that will help other children with [insert name of medical condition or subject matter of study] some day.

This study will not help you directly. We may learn something that will help other children with [insert name of medical condition or subject matter of study] some day.

Do you have to be in the study?

You do not have to be in the study. It is your choice to say yes or no. If you say no, no one will be mad at you. If you say yes and we start the activities, you can always change your mind and say no. We will ask your parent or caregiver if you can be in the study. Even if they say yes, you can still say no.

- Your parents/caregivers have also learned about what you will do. They have agreed to let you be in the study, if you want to do it.
- We will give you a squeeze ball when you are in the magnet. If you want to stop, you squeeze the ball and the machine will stop.

Do you have any questions?

If you have any questions, you can ask me now. If you think of a question later, you or your parent or caregiver can call me. My name is [insert name] and my phone number is [insert phone number]. If you want to talk to someone who is not part of the study, you can call Research Compliance Services at (541) 346-2510.

Do you want to be in the study?

Include instructions on how you want them to provide assent (examples below):

If you want to be in the study, please write your name on the line.



[or]

Shake your head or say yes if you do.

Assent for Research Participation (ages 12 to 17)

Template Assent Ages 12-17 may be found at irb.rap.uoregon.edu under the IRB > Library tab > Templates

Please add the following text to your document.

Today we are asking you to be in a research study. You can say yes or no. It is your choice. First, we will tell you about the study. Then we will ask if you want to be in it. You can ask any questions you want. We will also be talking to your parents or caregivers about the study. Even if your parents or caregivers say that it is okay for you to be in this study, you can still choose not to take part.

What is a research study?

A research study is a scientific way for people to learn things. We are trying to learn about [insert study purpose in simple language].

What will you do?

Describe all the research procedures using simple terms. If any parts of the study are experimental, explain those parts. Explain any medical terms or complex topics.

If you say you want to be in this study, you will be asked to do these things:

- Answer questions about [insert type of questions]
- Play some computer games
- Do some activities about words and sounds, kind of like what you do in school
- Have a small amount of blood taken from your [insert location of blood draw like arm or finger if blood sample will be taken].

This study will be done at the Lewis Center for Neuroimaging on the UO campus. A machine, called an MRI machine, allows us to look inside your body and brain using magnets to create computer pictures. The pictures can show us a lot of detail about different parts of your body and brain, and how they work when you are doing different tasks. No x-rays or material will be shot into your body of any kind in this MRI.

How long will it take?

We will see you [insert number of study sessions/visits]. Each time we see you, the visit will take [insert hours or minutes]. We can take breaks if you get tired. Just ask for a break.

Are there any risks?

Sometimes people feel tired or bored. If that happens, let us know and we will take breaks.

The stick from the needle to draw your blood may hurt a little, but the hurt will go away after awhile [Insert if blood draw is part of protocol].

Sometimes people do not feel good while being in this study. You might feel these things:

[List possible risks using language and length appropriate for this age group such as get embarrassed, get a headache, get a rash on your skin, get an upset stomach," etc.]. If you feel any of these things, or other things, be sure to tell your parent or caregiver and us.

There are safety rules to protect you from being hurt while in the MRI machine. We will ask you questions about any metal you may have on you or in you. This is to make sure you are not hurt. Depending on what you are wearing (like a shirt with metal buttons or pants with metal zipper), you may be asked to go into the bathroom and change some clothing and put on 'scrubs'. If you have metal on your body, such as rings, earrings, or other piercing, you will be asked to remove it. If you can not remove the metal, you will not be allowed to continue in the study.



The strong magnet in the scanner is more risky if some metal objects (like pens or paper clips or scissors) are brought into the room. There is a risk these objects may be pulled to the MRI or they may cause heating or burns to you. This can also occur if your body or our equipment are not positioned properly inside the MRI. We will carefully place you in the MRI with special pads.

The MRI scanner makes loud thumping, pounding and whining sounds during scans. These sounds may be annoying. You will wear headphones and/ or earplugs during the scan to protect your ears. You can bring your own earplugs from home or we will give you a set at the lab.

You may be nervous and/or tired by lying in the MRI machine. Some people are scared of small or enclosed places and may not like the scanner. If you want to get out you can tell us.

We [choose one: may/will] ask you to do a 'practice' session in our 'mock' scanner (which looks and sounds just like the 'real' scanner) before your session to see how you feel. You can also ask us if you want to do a practice session in our 'mock scanner'.

Before the scan starts we will give you a squeeze ball and show you on how to use it to stop the scan. If you want to stop while the machine is going, just squeeze the ball at any time to stop the scan. We will take you out of the machine.

Since you are under 18, your parents or caregiver have given permission for you to participate in the study. However, participating in the study is still your choice. You can refuse to be in the study even if you parent or caregiver said yes.

If you think you may be pregnant, you should not participate in this study. Although there are no known risks to having an MRI when pregnant, it is a time when the heart and brain are growing and we want to be extra safe. It's your choice. You can choose not to participate at any time and we will not ask for a reason why. We also won't tell your parent or caregiver why you didn't want to participate.

It is ok to stop participating in the study at any time. If you decided to stop, no one will be upset with you.

Include if there are physical risks to participation (otherwise remove):

Although we do not expect you to get hurt from being in the study it is possible that [describe what could hurt them]. Your parent(s) or caregiver(s) have been given information on what to do if you are hurt at any time during this study. If you are hurt, please tell your parent(s) or caregivers.

Are my answers private?

Describe how their information will be kept confidential. Explain situations where their private information may need to be shared with others. Include information about whether their information and/or samples may be shared with other researchers.

If you are in the study, we will keep your answers private. There are certain times when we have to tell someone what you said. The times we would have to tell someone else your answers are explained below.

- If we learn that someone has been hurting you or if we think you will hurt yourself or someone else, we may have to tell your parents or other adults because we want people to be safe.
- People who are paying for the study can ask to see your information and so can the people who review the study to make sure it's safe.

Sometimes people see or hear the answers that they shouldn't, but we will try very hard to not let that happen. We will take your name off of your answers whenever possible so only those who are supposed to have your information can see it. If the research involves the collection of identifiable private information and/or identifiable biospecimens, one of the following statements must be included:

When we take your name off of your answers, we might share that information with other researchers. -OR- Your information will only be used for this research and will not be shared with other researchers even if your name and other identifiable information is removed.



We store all of the pictures securely. Only people who are supposed to have access to your identifiable information will be able to know which pictures are of you.

If the minor will be receiving a pregnancy test because of the research, also include this language as applicable: After you are enrolled in this study and during the research, pregnancy testing will be performed. The result of the pregnancy test is confidential. We will tell you the result of the pregnancy test in private. Every effort will be made to maintain confidentiality regarding positive pregnancy test results. Whenever possible, we will not tell your parent(s) or caregiver(s) without your permission. However, under certain circumstances, we might be forced to reveal this information. For example, if your life or someone else's life was at risk or if abuse was suspected, it may be necessary to inform your parent(s) or caregiver(s) of a positive pregnancy test. If we believe it is necessary to tell your parent or caregiver of a positive pregnancy test without your permission, we will meet with you first in private to discuss our concerns before telling anyone any information about the pregnancy.

During the research, if you do have a positive pregnancy test, we may withdraw you from the study. This means that even if we do not reveal the results, your parent(s) or caregiver(s), may suspect that you are pregnant despite our best efforts to maintain confidentiality. If you become pregnant or if there is any chance that you might be pregnant (late menstrual period, broken condom, missed birth control pills, etc.) please contact the study personnel immediately.

If this study is NIH funded or otherwise has a certificate of confidentiality, include this language (otherwise, remove):

This study has an additional protection in place called a certificate of confidentiality. This protection limits the information that researchers can share with others who request personal information about you that includes your name or other identifiers for lawsuits or other court filings. Only researchers in this study will have information from this research study, unless there is a law that requires us to share the information (such as to report child abuse, communicable diseases, or harm to yourself or others). If you and your parents or caregivers give us permission, we could share this information for lawsuits or other court filings.

Additionally include the following language if has a certificate of confidentiality and is FDA regulated or if otherwise applicable (otherwise remove):

People who are in charge of the study and people who work to protect people like you who participate in research can still see your research information even with the certificate of confidentiality. This includes [THE AGENCY] which is funding this project [and/or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA)]. The certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to someone outside of the study like your doctor, or any other person not connected with the research, you and your parents or caregivers must give us permission to share that information.

Language such as the following should be included if researcher intends to disclose information covered by a Certificate, with the assent of research participants:

If you and your parents or caregivers give us permission to share information from this research with other people, like your doctor, the certificate of confidentiality won't stop us from doing that.

Are there any benefits?

Explain any possible direct benefits to the child posed by the research using simple terms. If you don't know if they will benefit or if there are no benefits to them directly, state that using simple terms.

We do not think you will benefit directly from being in our study, but you will help us learn more about [reiterate purpose].

We do not know if you will be helped by being in this study. We may learn something that will help other children with [insert name of medical condition or subject matter of study] some day.

This study will not help you directly. We may learn something that will help other children with [insert name of medical condition or subject matter of study] some day.



Will I get anything?

Explain any payments or incentives they will receive. If there are none, remove this section. If you decide to be in the study, you will receive [insert compensation information].

Do I have other choices?

Describe any alternative procedures that might be available to the child other than this study. For example, for educational research, maybe the alternative is to do some other type of classwork; or for clinical research, maybe the child can still see their clinician, but their information won't be used for research. If none, this section can be removed. If you do not want to be in this study, you can say no. If you say no to being in this study, you will [insert alternatives if any to participation].

Do you have to be in the study?

You do not have to be in the study. It is your choice to say yes or no. If you say you do not want to be in the study, no one will be upset with you. You won't be punished for saying no and you won't lose any benefits you already get. If you say yes and start the study, you can always change your mind later and stop being in the study. You can say no even if your parent or caregiver said you can be in the study.

Do you have any questions?

If you have any questions, you can ask me now. If you think of a question later, you or your parent or caregiver can call me. My name is [insert name] and my phone number is [insert phone number]. If you want to talk to someone who is not part of the study, you can call Research Compliance Services at (541) 346-2510.

Do you want to be in the study?

If you want to be in the study, please write your name on the line.

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Appendix C: Pregnancy Task Force Document

Overview

The goal of this document is to provide background and guidance as part of a 'task force' to examine current knowledge of the effect of magnetic resonance imaging (MRI) on pregnancy. The task force will provide guidelines to help the UO IRB evaluate protocols run at the Lewis Center for Neuroimaging (LCNI) based on the most up to date scientific information available behind the safety of MRI during pregnancy.

This document was created by task force members: Fred Sabb, the previous Director of the LCNI and an active member of the brain mapping community, created the initial draft of this document, which was subsequently edited by Deanne Unruh and Sheryl Johnson of Research Compliance Services, and then by two outside experts: Colin Studholme of University of Washington, who conducts fetal imaging experiments and Susan Bookheimer of UCLA, who was a member of the 2005 NIH Council that developed the last set up guidelines and is currently Director of the UCLA Staglin MRI Center.

The scope of this document is decidedly narrow: Specifically, what are the potential risks of pregnancy in MRI, and do those risks affect mother or fetus? From this scope, we developed guidelines, which will be presented in an open forum to all IRB members.

Background

Magnetic resonance imaging works through the interaction of hydrogen nuclei with external magnetic fields. When an object containing hydrogen is placed in an MRI machine, the very strong magnetic field produces a weak polarization. Although this polarization is very small, summing over the large number of hydrogen atoms in most biological tissues produces a measurable effect. Radio-frequency electromagnetic pulses are then applied in a predictable sequence, producing a response that depends on the local magnetic environment and that can be used to build images of the object. Because the local magnetic environment is affected by physiologic processes such as blood flow and oxygenation, MRI can be used to noninvasively examine brain function.

MRI has been in clinical use since the early 1980's. Functional MRI has been used in humans for over 20 years. In 1998, the FDA announced that devices with static field strengths up to 4 Tesla would be considered low risk devices, and recommended caution when scanning pregnant patients. In 2002, the FDA approved several 3Tesla MRI scanners for whole body imaging. The most recent (2014) guidance document from the FDA states that static fields up to 4T for neonates and 8T for adults and children over one month old are considered to constitute low risk, and makes no mention of special considerations during pregnancy. Over 13,000 MRI scanners are in operation globally, including hundreds of research scanners dedicated to functional imaging.

The primary guidelines provided by the NIH to IRBs for MRI practices followed a Council work-group meeting in 2005. (<http://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/mri-research-safety-ethics.pdf>). This comprehensive document discusses everything from physical set up of the scanner and center, to training for individuals and safety considerations, particularly in regard to MRI centers not affiliated with a medical school.

This document presents pregnancy as having 'no known risk' associated with MRI scanning, and furthermore accurately states that there are no known mechanisms of potential risk under normal operating procedures. However, because future studies could possibly show some risk to pregnancy, the exclusion of pregnant participants is justifiable. This opinion has been shared with me by two members of the panel, one of whom, Dr. Bookheimer, has provided her editing of this document: there was no known risk and no known mechanisms of risk, but that women who believe they may be pregnant may choose not to participate.

The other document that the UO IRB currently uses as a supplementary guideline for MRI is the 2013 guidance document on MR safe practices from the American College of Radiology (JMRI 37:501-530, 2013). This document is written primarily by radiologists and concerns clinical implementations. Thus, it is concerned only with the direct benefit/risk to the patient, and does not address human subjects in a research setting. Nevertheless, it takes a similar position as the previous document: no study has shown a negative effect of MRI to a developing fetus, however, delaying MRI until after pregnancy



if possible is considered prudent.

Current Knowledge

A number of studies have been performed in animals and humans during pregnancy to answer novel questions about pregnancy and fetal development as well as to explicitly test safety. These studies show the risk for scanning during pregnancy is no greater than that of MRI in any individual, once certain manufacturer and FDA provided precautions are taken. In our review below, we have specifically looked for reports of adverse findings and targeted review articles as frequently as possible that could present an objective review of the literature.

The physics behind MRI only allows for three potential paths for risk: heating, sound, and the static field itself, with the only applicable risk for our 3 Tesla scanner coming from interactions with ferromagnetic devices. MRI at 3T is FDA approved and considered a “minimal risk” for children and adults under normal operating procedures. Once precautions are taken to minimize risk due to ferromagnetic objects near the magnetic field (as they are with all studies here at the UO and everywhere), there are two remaining issues for potential participants: the potential for heating due to radio-frequency energy deposition and excessive noise from gradient switching. Of note, the 2005 NIH guidelines sets limits for infants, children, and adults in these areas. They did not provide guidance on these limits for the fetus. Around the same time, preeminent MRI safety expert, Frank Shellock (and Crues) reviewed the literature in 2004 and found “there is no substantial evidence of injury or harm to the fetus; however, additional research on this topic is warranted”.

Both heating and noise have been examined carefully prior to this meeting and over the last 9 years in both animal and human studies, showing these risks are not elevated for mother or fetus in pregnancy. Studies examining negative outcomes have followed children up through 9 years of age, finding no ill effects (Chen et al).

No disability related to MR exposure has been detected in follow-up studies of infants and children who had been exposed to MR imaging in utero [1,2]. Additionally, MR exposure at early embryonal stages has not been associated with a higher risk for adverse fetal health or reproductive outcomes in studies of pregnant female MR workers [3,4] and patients [6]. Additionally, no abnormalities in hearing function has been observed in follow up studies of infants and children who had been exposed to MR imaging in utero [1,2], partially due to the fact that MR noise is grossly absorbed by amniotic fluid [5]. Other basic biological studies have also revealed no negative impacts of MRI exposure [7,8,9].

Levine and colleagues (2001) examined heating effects in pregnant pigs, using fast MR-imaging and fiber optic probes. The authors report “no heating occurred in fetal tissues or amniotic fluid”. Gowland and De Wilde (2008) report radio-frequency absorption rates (SAR) deemed acceptable using previous research in sheep and mathematical modeling of heat deposition in utero. Hand and colleagues (2010) conducted similar research in humans, similarly finding no ill effects and developing parameters for safe MR scanning during pregnancy (Hand et al., 2010; Kikuchi et al. 2010). Kikuchi et al. demonstrate that one can safely scan for up to 40 minutes without raising the internal temperature of body core or the fetus above the 0.5 degree Celsius (~0.9 degrees F) FDA-recommended limit using SAR of 2.0 W/kg.

Examination of sound has similarly shown that there is no increased risk to the fetus under normal operating parameters for MRI as approved by the FDA. Glover et al. (1995) used a fluid-filled model uterus in order to assess the sound level experienced by the fetal ear during maternal MRI, and found a better than 30 dB attenuation. This is enough to reduce MRI noise to a safe level, with peak pressures below those obtained by tapping the abdomen with the fingers.

Patenaude and colleagues (2014) very recently reviewed the literature as part of a Diagnostic Imaging Committee for Obstetricians and Gynecologists in Canada. They note that the only three early animal studies from the late 1980s and early '90s in mouse and chick development during the first trimester have raised concerns about miscarriages and eye-malformations putatively related to prolonged exposure to MRI at 4T. Follow-up work however questioned the applicability of these early models to human systems, as heating in the human womb is negligible with clinically relevant scanning protocols (Chen MM and colleagues 2008). Patenaude and colleagues summarize that ‘Fetal MRI is safe at 3T or less during the 2nd and 3rd trimesters’ and that “Inadvertent exposure to magnetic resonance imaging during the first trimester has not been associated with any long-term sequelae and should not raise clinical concern”. But they and others note that caution should be exercised during scanning within the first trimester. Finally, they also note that other reviews of safety by



Shellock (2004) and the ACR do not distinguish between trimesters in their assessment of safe practices in MRI.

Best practices currently in the literature for setting SAR and noise limits for safe imaging of the fetus are based on the studies listed above and others. Thomason and colleagues (2013) provide a substantial background, which was instrumental in identifying the current knowledge base. Best practice currently in the literature for setting SAR and noise limits for safe imaging of the fetus are based on a number of studies, and summarized well in their report. Recommendations for children and adults, based on the FDA guidelines and the 2005 Council are that a maximum limit of 2 Watts per kilogram is allowed, which corresponds to a safe allowance in heating of about 0.5 degrees Celsius. A number of studies have shown that this represents a safe allowance for the fetus as well; however, a more conservative limit may be used for fetal imaging. The Thomason report demonstrates that developing protocols that reduce SAR to less than 0.6 W kg^{-1} is possible.

It is also important to consider the risks associated with either testing for pregnancy or excluding individuals who could potentially be pregnant by investigator, rather than subject identification. In the former case, there is risk in identifying pregnancy in a teen that is unknown to either the teen or the parent. In such a case there may be a legal mandate that conflicts with subject safety and with confidentiality, and may produce negative, possibly serious, psychological harm. In the latter case, eliminating a class of individuals such as teenage may constitute discrimination. These issues were considered in the 2004/5 working group, and identified risks of pregnancy testing or discrimination on the basis of potential pregnancy in the absence of a known MRI risk were thought to outweigh the potential benefits of testing or discrimination.

Proposed LCNI policy

Our center policy for all studies will be to properly and fully inform participants of current best practice and, whenever feasible, strongly recommend participants choose to exclude themselves if they are or may be pregnant. For almost all research studies, this will not adversely affect the research approach. We think it is important this is an informed choice by participants and not an exclusion, which may (and has in the past) lead to prejudice against research benefits for women of child bearing age.

For studies involving vulnerable populations, we will use an enhanced screening procedure that gives individuals an easy and anonymous way to opt out of the study at several points, without divulging a reason and provide explicit and highlighted language in assent/consent forms that any chance of being pregnant should lead to exclusion. Minors will have a chance to meet privately with the researcher (without a parent/guardian present). It is our center policy and that of a number of other centers (including UCLA) that conducting pregnancy tests is more invasive than unintended exposure of the fetus to MRI at 3T.

In rare cases where scanning women who are pregnant is essential to the research question, we will work with the IRB to apply the guidelines below to ensure the highest possible ethical standards for conducting research at the UO.

For conducting studies that explicitly seek to involve MRI during pregnancy, LCNI guidelines are as follows (based on UW approved protocol from Dr. Studholme):

In all MRI studies, a number of precautions must be taken. On top of our standard operating procedures for safely conducting MRI, which includes pre-screening and interview-based screening in order to identify and resolve any potential source of risk from the participant, SAR limits that are appropriate for the fetus must be followed. These limits are different for adults and children and set as part of manufacture and FDA guidelines for proper use. Not only is the expected SAR calculated before the scan can be started, but energy deposition is continuously monitored during scanning and the scan is halted if this value approaches the FDA limit. It should be noted that the sequences used in functional MRI are low SAR sequences, typically exposing the subject to less than 20% of the FDA limit. Our policy will be to follow guidelines set by Thomason and colleagues for developing scanning parameters that keep SAR under 0.68 W/kg .

Only babies that are beyond the first trimester of pregnancy (typically greater than 18-19 weeks), which is after the time when major organs such as the heart, have already formed, and the brain is large enough to collect meaningful images, will be scanned. By following the above guidelines our modified imaging protocol does not change the electromagnetic behavior of the system in a way that would impact the fetus more than standard approved clinical imaging. Only women who are having a healthy pregnancy will be included. We will require studies conduct a follow-up questionnaire with participants after



they have given birth.

Having just returned from one of the preeminent conference for brain mapping, the Organization for Human Brain Mapping, it is clear to me that prenatal MRI research will continue to grow, with some researchers even referring to it as the 'Big Bang' of brain development research. Developing a consensus set of guidelines as laid out here will be helpful for both researchers and the IRB in moving forward on this very important issue.

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