

CARILION CLINIC INSTITUTIONAL REVIEW BOARD

Standard Operating Guidelines

Title: 4.3: Guidelines for Researchers Using Gadolinium-Enhanced MRI in Research	
Original Date: July 9, 2010	Revision Date: 8-23
Primary Sponsor: Human Research Protections Office	Approved By: Director of the Human Research Protections Office

Objective:

To set forth guidance for researchers regarding use of gadolinium-enhanced MRI in research and establish acceptable language for use in research protocols and informed consent documents.

General Guidance:

In general, the use of gadolinium-enhanced MRI for research purposes will not be approved in subjects with an estimated GFR of less than 45 mL/min. The lab values used to calculate the GFR must be drawn within 30 days of the planned study MRI and the principal investigator must describe a method of screening for new onset kidney problems the day of the exam. For example, the subject should be given a questionnaire about new onset of kidney problems the day of the exam.

For studies which utilize gadolinium-enhanced MRI the protocol and consent must list the risk of Nephrogenic Systemic Fibrosis (NSF.)

In 2006, the FDA released a warning about this new and rare disease that is linked to the use of gadolinium. The warning is most relevant to people with severe chronic kidney disease (with GFR less than 30 mL/min), end-stage kidney disease (with GFR less than 15 mL/min), including those requiring dialysis. The warning is also relevant to people with acute kidney injury, hepato-renal syndrome, in the perioperative liver transplant period, or have a history of paraproteinuria syndromes such as multiple myeloma.

NSF causes fibrosis of the skin, connective tissues like muscles, tendons, ligaments, and blood vessels throughout the body. In addition, those who develop NSF may have scarring of their vital organs. The signs of NSF include:

- burning, itching, swelling, hardening and tightening of skin;
- red or dark patches on the skin;
- yellow spots on the whites of the eyes;
- stiffness of joints with trouble moving or straightening the arms, hands, legs or feet;
- pain deep in the hip bones or ribs;
- muscle weakness

Protocol Language:

Exclusion Criteria for protocol using gadolinium-enhanced MRI in research:

Add the following criteria to the protocol under the inclusion/exclusion criteria:

- estimated GFR less than 45 mL/min based on a serum creatinine drawn within 30 days of the MRI

- acute kidney injury
- history of paraproteinuria syndromes such as multiple myeloma
- hepatorenal syndromes
- liver transplant
- pregnancy

Required Risk Language for the Protocol Using Gadolinium-Enhanced MRI for Research:

Place this information in risk section of the protocol:

An extremely rare disease called Nephrogenic Systemic Fibrosis (NSF) is linked with the use of gadolinium in people with:

- severe chronic kidney disease (with Glomerular Filtration Rate (GFR) less than 30 mL/min)
- end-stage kidney disease (with GFR less than 15 mL/min) including those requiring dialysis

NSF causes hardening and thickening (fibrosis) of the skin, connective tissues like muscles, tendons, ligaments, and blood vessels throughout the body. In addition, those who develop NSF may have scarring of their body organs. NSF may be progressive (may worsen) and may be fatal. There is no known treatment for NSF. Skin biopsy is the only true means of diagnosis.

In addition to the exclusion criteria in this protocol, all subjects will be screened by the Department of Radiology staff prior to receiving gadolinium. If radiology screening indicates that it might be unsafe for a subject to receive this contrast, then the subject should not be given the contrast for research purposes and the subject will be immediately withdrawn from the study.

Consent Language

Required Risk Language for the “What Will Happen in this Research” Section:

If you decide to take part, you will be asked to have a DE-MRI exam (please state how many, when and what area of the body) The DE-MRI will look at (please state purpose of the scan.)

MRI makes images of your body by using magnetic fields and radiowaves. The MRI exam will take approximately 30-45 minutes. Prior to your exam, you will be asked to complete a standard questionnaire. The purpose of this questionnaire is to ensure that you are able to safely enter the MRI area. You will also be asked to give a urine sample for a pregnancy test if you are a woman of childbearing potential.

To start your MRI test, you will lie on a padded table. An intravenous catheter (IV) will be placed in an arm vein during the study. This is to inject the contrast agent, Gadolinium, during the scan that highlights specific areas of interest.

The table on which you are lying will be moved to the center of an MRI magnet, which looks like a long narrow tube. Even though the tube is open, some people feel confined in small places. If this bothers you, please notify the MRI staff. You may end your participation in this study at any time by telling the MRI staff. When MRI pictures are taken, radio-signals and magnetic fields are used. When this happens, it is normal for the MRI machine to make loud, banging, and clicking noises. You will be asked to wear earplugs or headphones for your comfort during the exam. During the exam, the MRI staff is able to see and hear you through an intercom. The MRI staff will be talking to you throughout your MRI exam and may issue simple instructions regarding holding your breath, maintaining position, etc. You will generally be requested to lie perfectly still throughout the exam. You will be able to speak with the staff prior to the scan but while the scan is running you will not be in voice contact. To contact the staff during the scan you will be given a squeeze bulb.

You can squeeze the bulb if you need to get the staff's attention. The scan will be stopped and the staff will be able to talk to you.

Required Risk Language for the "What are the Risks to Being in this Research" Section:

As part of the MRI/MRA you will receive a contrast called Gadolinium. This substance will help the tissues show up better. The FDA has received information about a new and extremely rare disease called Nephrogenic Systemic Fibrosis (NSF) that is linked with the use of Gadolinium in people with severe kidney disease.

NSF causes hardening and thickening (fibrosis) of the skin, connective tissues like muscles, tendons, ligaments, and blood vessels throughout the body. In addition, those who develop NSF may have scarring of their body organs. The signs of NSF also include:

- burning, itching, swelling, hardening and tightening of skin;
- red or dark patches on the skin;
- yellow spots on the whites of the eyes;
- stiffness in joints with trouble moving or straightening the arms, hands, legs or feet;
- pain deep in the hip bones or ribs;
- Muscle weakness.

In most of the cases reported to the FDA, symptoms of NSF started between 2 days to 18 months after a person received the Gadolinium-based contrast agent. NSF may get worse and may lead to death. There is no known treatment for NSF.

IF you have any of the symptoms listed above after receiving Gadolinium-based contrast for a study MRI/MRA, please contact the study team immediately. The study team will review your symptoms and perhaps recommend a skin biopsy, which is the only way to determine if you actually have NSF.