

F. M. Kirby Research Center for Functional Brain Imaging

Kennedy Krieger Institute

Baltimore, Maryland

## Policy & Procedures / Safety Manual

9 August 2001

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Safety Officer,  
Kennedy Krieger Institute

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Safety Officer,  
F.M. Kirby Research Center  
for Functional Brain Imaging

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President,  
Kennedy Krieger Institute

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## I. ORGANIZATION

### A. INTRODUCTION

The F. M. Kirby Research Center for Functional Brain Imaging (KRCFBI) at the Kennedy Krieger Institute (KKI) is a research center, which with respect to safety, falls under the general auspices of relevant institutional policies at KKI, the Johns Hopkins University, and other relevant policy-making bodies and organizations. This manual serves as a supplement to safety regulations and policies already established, and is concerned only with safety policies unique to the KRCFBI, principally due to its specialized facilities for studies using magnetic resonance imaging (MRI) and spectroscopy methods.

MR systems in the KRCFBI shall be operated in strict adherence to existing guidance from the Food and Drug Administration (FDA) for magnetic resonance diagnostic devices. All investigators using MR systems in the KRCFBI are responsible for insuring that their use of these systems will be in strict adherence to these guidelines.

Any categories not included in this document (*e.g., the treatment of biohazards, laboratory safety for chemicals, etc.*) are referenced to the relevant guidelines and policies governing other clinical and research facilities at KKI. In the event of a conflict between this document and these guidelines/policies, this document preempts these.

### B. THE KRCFBI PROTOCOL REVIEW COMMITTEE

The KRCFBI Protocol Review Committee comprises individuals knowledgeable about experimental procedures in MR, medicine, physiology, chemistry, physics, and electronics.

The KRCFBI Protocol Review Committee (PRC) is responsible for the review and approval (or disapproval) of protocols for all research uses of the KRCFBI. This committee supplements, and in no way replaces, the Institutional Review Boards (IRB) of the Kennedy Krieger Institute, the Johns Hopkins University, and the University of Maryland. Research protocols should be submitted first to the appropriate IRB, and approval obtained, before submission to the KRCFBI PRC. Research is not to be conducted within the KRCFBI without approval of both the PRC and the IRB.

The PRC is ultimately responsible for safety within the KRCFBI, and will perform the following safety-related tasks:

1. Review all protocols for conformance to the provisions of the KRCFBI Safety Policy.
2. Revise the KRCFBI Safety Policy as needed; review the safety manual periodically.

3. Appoint a KRCFBI Safety Officer, who must be a member of the KRCFBI Protocol Review Committee.
4. Convene at least four times a year, but usually monthly.

In the event that an unsafe condition arises, or the safety policy is violated, the PRC has the responsibility to revoke approval of the protocol involved until the condition is corrected. The Protocol Review Committee Chair and the KRCFBI Safety Officer have this authority *pro tempore*.

### C. KRCFBI SAFETY OFFICER (SO)

The KRCFBI Safety Officer (SO) is a member of, and is appointed by, the KRCFBI Protocol Review Committee. He/she is a qualified scientist with knowledge of the operation, safety hazards, and safety policy of the KRCFBI. He/she has the authority to suspend any activity in the KRCFBI that, in his/her judgment, violates the KRCFBI Safety Policy, or otherwise constitutes an unsafe condition. He/she may transfer this authority to an approved Operator of the facility. The SO will perform the following safety-related tasks:

1. Ensure that the provisions of the KRCFBI Safety Policy are carried out in the execution of approved laboratory protocols.
2. Advise the KRCFBI PRC as to needed changes in KRCFBI Safety Policy.
3. Coordinate classes concerning safe conduct in the KRCFBI.
4. Verify that any personnel involved with any function of the KRCFBI have attended the aforementioned safety class.
5. Maintain a permanent file of incident reports and any corrective actions taken.
6. Ensure adequate distribution of this manual governing Safety Policy.
7. Maintain safety records of KRCFBI Operators.
8. Report monthly to the Chair of the KRCFBI PRC and quarterly to the Safety Committee of the Kennedy Krieger Institute.
9. Remain current on all new governmental and non-governmental safety policies and recommendations.
10. Maintain the video tape on MR safety; make it available for viewing; and maintain records of its viewing by individuals.

## D. OPERATORS

An Operator of the KRCFBI will be certified as such once he/she has:

1. Obtained a bachelor's or master's degree in physics, radiology, neuroscience or a related discipline; and satisfactorily completed both a formal class on MRI scanner operation and a formal class on safety, both administered by the KRCFBI SO (the formal class of MRI may be waived if adequate previous experience and/or course work in MRI can be demonstrated).
2. Viewed the video tape on MR safety within the past year.
3. Been approved by the KRCFBI Protocol Review Committee.

A certified Operator in the KRCFBI understands that safe operation within the KRCFBI and the administration of this safety policy is his/her responsibility while he/she is present in the KRCFBI.

Any violation of this policy will be documented in writing by the Operator and submitted to the SO within 24 hours of the incident.

## E. RESEARCH PERSONNEL

Personnel will be permitted in the KRCFBI scan room (for the purpose of performing studies approved by their IRB and the KRCFBI, and scheduled for scanning) once he/she has:

1. Viewed the video tape on MR safety within the past year.

## II. KRCFBI SAFETY POLICY

### A. INTRODUCTION

The F. M. Kirby Research Center for Functional Brain Imaging (KRCFBI) at the Kennedy Krieger Institute houses a 1.5 Tesla MRI system manufactured by Phillips Medical Systems of the Netherlands.

This system has been approved by the FDA for human examinations. It incorporates the following equipment:

1. A superconducting magnet, shim coils, gradient coils, and transmitter/receiver radiofrequency (RF) coils.
2. A computer controlled MR spectrometer incorporating an RF transmitter/receiver system and gradient and shim power supplies. The spectrometer controls the timing of RF and gradient pulses, the acquisition of MR data, and the processing, display and storage of the MR data.

### B. DEFINITIONS

### 1. Nuclear Magnetic Resonance (NMR):

Nuclear Magnetic Resonance is a phenomenon of an ensemble of nuclei of an isotope with non-zero ground state spin angular momentum. When the ensemble is placed in a magnetic field, the nuclear ground state energy is split into  $2I+1$  different states, where  $I$  is the nuclear spin of the ground state. The energy difference between the states is linearly dependent on the local magnetic field and the nuclear gyromagnetic ratio. A resonant absorption appears when a radiofrequency electromagnetic signal is transmitted to the nuclei at their resonant frequency. The frequency of resonance is known as the Larmor frequency.

### 2. Magnetic Resonance Imaging (MRI):

Any one of numerous techniques which utilize as a basis the pulsed NMR experiment to produce a signal proportional to: a) nuclear spin density, and/or; b) a function of nuclear spin density and nuclear relaxation times. Magnetic gradient fields and radio-frequency fields are pulsed in one of several sequences so that the acquired signals contain spatial information as well as nuclear spin density and quantities related to the local physical properties of the material being imaged. The acquired signals are analyzed to produce an image of the sample in some plane of interest.

### 3. MR Spectroscopy:

Any one of numerous techniques which utilize a pulsed NMR experiment to produce a spectrum. The magnitudes of the resonance signal areas of the spectrum depend on nuclear density and nuclear relaxation times. The positions of the resonance signals are based on the fact that the shielding and deshielding of atomic shell electrons causes nuclei in different positions within the same molecule to have slightly different Larmor frequencies (chemical shifts). These chemical shifts and resonance signal areas can be used to ascertain information about the molecule.

### 4. Restricted Access Area:

The KRCFBI is a restricted area.

### 5. High Magnetic Field:

Any static magnetic field in excess of 50 gauss (0.0005 T).

### 6. Scan Room:

The room containing the 1.5 Tesla Phillips magnet.

## C. HAZARDS

Potential hazards to subjects during MRI examination include:

1. Static magnetic fields
2. Pulsed gradient magnetic fields
3. Radiofrequency electromagnetic fields
4. Acoustic noise

Incidental hazards to Operators and subjects in the scan room include:

1. The subject may have implanted objects which might dislodge (*e.g., an aneurysm clip*), or malfunction (*e.g., a pacemaker*), or become attached to the magnet (*e.g., a metal pin*) in high static magnetic fields.
2. It is possible for a person to become trapped between the cryostat and a magnetic object. If the object is fairly massive (*e.g., a pound or more*), forces of up to 150 pounds may be generated for every pound of ferromagnetic material. The person may thus be subjected to severe force and mechanical stress.
3. The cryostat of the magnet contains several hundred liters of cryogenes. If the magnet quenches, (*i.e., makes the transition from superconducting to resistively conducting*) the liquid helium in the innermost cryostat will boil off rapidly, and, in the (unlikely) event of failure of the helium discharge duct, may displace oxygen in a closed environment, leading to an asphyxiation hazard.

#### D. SAFETY STANDARDS FOR HUMAN MR STUDIES

##### 1. General:

MR systems in the KRCFBI shall be operated in strict adherence to existing guidance from the Food and Drug Administration (FDA) for magnetic resonance diagnostic devices.

##### 2. Static Magnetic Field Strength:

The 1988 FDA Guidance and Safety Parameter Action Levels indicate that static field strengths of up to 2 Tesla comprise nonsignificant risk to human subjects. The systems to be used for human studies operate within these limits.

As with any human research study, those using this magnet will only be performed after approval from the appropriate Institutional Review Board (IRB) and the KRCFBI/PRC. If new limits on human exposure to magnetic fields are defined in the future, the KRCFBI will immediately comply with these limits.

### 3. Gradient Switching:

Safety parameter action levels on the rate of change of magnetic field strength will be adopted as limits in our human studies. These were established in 1988 as follows:

a. Demonstrate that the maximum dB/dt of the system is 6 T/second or less: **BELOW LEVEL OF CONCERN**

OR

b. *For axial gradients:* If  $dB/dt < 20 \text{ T/s}$  for  $\bullet \geq 120 \text{ ms}$ , or  
if  $dB/dt < 2400 \bullet \bullet \bullet (\text{ms}) \text{ T/s}$  for  $12 \text{ ms} < \bullet < 120 \text{ ms}$ , or  
if  $dB/dt < 200 \text{ T/s}$  for  $\bullet < 12 \text{ ms}$ , and

*For transverse gradients:* If dB/dt is less than 3 times the above limits for axial gradients:  
**BELOW LEVEL OF CONCERN**

OR

c. Demonstrate with valid scientific evidence that the rate of change of magnetic field for the system is not sufficient to cause peripheral nerve stimulation by an adequate margin of safety (at least a factor of three): **BELOW LEVEL OF CONCERN**

The parameter dB/dt cited above must be shown to fall below either of the two levels of concern by presentation of valid scientific measurement or sufficient calculational evidence must be provided to demonstrate that the time rate of magnetic field change (dB/dt) is of no concern.

Levels exceeding this need to be evaluated in terms of the likelihood that they may produce painful nerve stimulation. The FDA Guidance (1995) was developed specifically to consider the fact that many clinical systems were capable of exceeding these levels of dB/dt. It was originally considered that a warning level should be implemented to guard against peripheral nerve stimulation, but it was concluded that: "... this warning level is not considered critical since there are no harmful effects associated with mild peripheral nerve stimulation" (FDA Guidance, 1995). The current guidelines therefore include monitoring procedures to help avoid painful peripheral nerve stimulation, without specific dB/dt limitations.

We will consider any study that could exceed the level of concern as identified in the 1988 guidance, and in those cases implement the recommendations of the FDA for monitoring peripheral nerve stimulation. Following the FDA Guidance (1995), our system will generate a special notification below the lowest dB/dt level at which peripheral nerve stimulation has been observed in volunteer and clinical studies (in fact, we will use the level of concern described in the 1988 Guidance to implement these notifications, which is more conservative than the FDA guidelines). Deliberate action by the operator will be necessary to proceed with a scan in these cases. System operators will also receive special training, and before any scanning procedure that

might stimulate peripheral nerves, operators will:

- i. inform the subject that peripheral nerve stimulation may occur,
- ii. describe the nature of the sensation to the subject,
- iii. instruct subjects not to clasp their hands, since this may create a conductive loop which will increase the possibility of stimulation,
- iv. maintain constant contact with the subject,
- v. instruct subjects to inform the operator if they experience severe discomfort or pain,
- vi. terminate the scan if the subject complains of severe discomfort or pain,
- vii. complete a report of any incidents involving severe discomfort or pain, including a description of the associated circumstances (imaging parameters, dB/dt value, level of pain, etc.), and submit this report immediately to the MRI Laboratory Safety Officer. The individual investigator is responsible for reporting any incidents to their IRB.

All consent forms for studies that might induce peripheral nerve should include language providing this information, and operators will administer an exit questionnaire, using terms and explanations for key symptoms (e.g., vertigo) in language that subjects can understand. A record of dB/dt value should also be included with the image data, to help in analysis of levels of peripheral nerve stimulation possibly perceived by subjects.

#### 4. Specific Absorption Rate (SAR)

Safety parameter action levels on specific absorption rate (SAR; i.e., possible heating associated with absorption of radiofrequency [RF] energy) will also be adopted as limits in our human studies. These are summarized as follows:

Options:

- a. If SAR < 0.4 W/kg whole body:  
and if SAR < 8.0 W/kg spatial peak in any 1 gram of tissue,  
and if SAR < 3.2 W/kg averaged over the head:  
BELOW LEVEL OF CONCERN

OR

- b. The SAR parameter for RF heating cited above must be shown to fall below either of the two levels of concern by presentation of valid scientific measurement or calculation evidence sufficient to demonstrate that RF heating effects (SAR) are of no concern.

#### 5. Acoustic Noise:

Acoustic noise levels must be shown to be below the level of concern established by pertinent Federal Regulatory or other recognized standards setting organizations. If the acoustic noise is not below the level of concern, steps to reduce or alleviate the noise perceived by the subject must be taken.

## E. ACCESS

Access to the KRCFBI will be controlled, allowing access for only personnel, escorted visitors, and research subjects who have legitimate reason to be in the restricted area. Entry into the scan room is further restricted. The purpose of controlling access to the scan room is to control the entry of ferromagnetic and other materials which might cause injury to research subjects, personnel, or equipment.

1. Access to the KRCFBI Scan Room will be restricted to those individuals authorized by the KRCFBI Protocol Review Committee. The SO has the duty to restrict access to only those personnel, and to eject individuals acting in an unsafe manner.
  - a. To assure their safety, no research personnel shall be allowed into the scan room unless they have viewed the video tape presentation on MR safety.
  - b. To assure their safety, KKI Security staff will have access to the scan room of the KRCFBI only under the supervision of the SO or a qualified Operator. In the event of an emergency, the Security Officer must attempt to contact the SO or a qualified Operator before entering the KRCFBI scan room. Once contacted, the SO will direct the Security Officer in safe methods to access the scan room, and safe procedures to follow once the scan room is entered. All unauthorized personnel are barred from the high field area.
  - c. Only specially trained housekeeping staff will have access to the scan room of the KRCFBI.
2. The Operator will question and inform all individuals requesting entrance to the KRCFBI scan room of specific safety hazards related to exposure to high magnetic fields.
3. Magnetic objects will not be allowed into the KRCFBI scan room unless prior arrangements have been made.
4. Any person who has previously had surgery may be subjected to metal detection examination either by x-ray or a metal detector before entering the KRCFBI scan room.

## F. FACILITIES

1. The KRCFBI will be properly ventilated to evacuate excess nitrogen and helium gasses. Ventilation will be adequate to provide fresh air on a regular basis and to remove the heat load generated by the equipment.
2. There will be a separate helium discharge duct for each MR system.

## G. ELECTRICAL

1. All modifications to the equipment will be performed only by qualified personnel and will be properly evaluated in terms of electrical safety.
2. Research subjects, Operators, and other individuals will not have direct contact with MR coils.

## H. CRYOGENS

1. The transfer of cryogenics and all handling of dewars and cryogenic substances will be performed by qualified personnel with experience in cryogenics, using only non-magnetic equipment and containers tested and designed for cryogenic use. In particular, transfer lines should be made of latex, non-ferromagnetic metal or other shatter-resistant material.
2. Individuals will wear suitable face and hand protection when transferring cryogenics.
3. Dewars shall be checked for correct pressure and ventilation before and after liquid transfers.
4. All dewars, particularly liquid helium containers, must be kept sealed and under a slight positive pressure at all times.
5. Each MR system will have in place a venting system, triggered by high cryogenic flow rate, to carry cryogenics out of the facility rapidly if a quench should occur. In the event that a helium quench does occur, any human subject (if present) must be removed from the system, and with all other personnel, will evacuate the area immediately.

## I. SIGNS AND WARNINGS

Each restricted access area will be posted with conspicuous signs advising of the existence of high magnetic fields. The signs must contain warnings to wearers of pacemakers, as well as general warnings against carrying magnetic materials into the facility. In addition to warning signs, the name, work extension, and home phone numbers of the SO and other backup Operators will be posted conspicuously on the laboratory door. This information will also be provided to KKI Security.

1. The entrance to the scan room will be posted with "Do not enter" warning signs describing the hazards of entering the area.
2. Anyone who is not an Operator and who wishes to enter a restricted access area will be questioned and advised of the known hazards.

3. Potential research subjects will be fully informed as to the risks, hazards, procedures, and possible emergencies involved in their studies in the KRCFBI. The specific procedures for informed consent fall under the purview of, and must be approved by, the KKI/IPC IRB.

## J. FIRE

### General:

1. Necessary equipment (fire extinguishers, etc.) will be provided to manage all classes of fire. All equipment will be non-magnetic.
2. No flammable liquids in excess of five gallons will be brought into the KRCFBI.

### Fire with Operators on site:

1. The Operator will know all of the fire emergency related procedures, including a subject evacuation plan, and its proper execution.
2. In the event of a fire in the scan room requiring outside response, the Operator will perform an emergency quench of the magnet by activating the emergency magnet shut-off.
3. In the event of a scan room fire requiring outside response, the SO and Operators will direct fire fighting operations until such time as the magnetic field reaches zero.

### Fire with no Operators on site:

1. Once contacted, the SO or alternate Operator will instruct fire fighting personnel and/or Security staff as to means of entry and to the proper means of quenching the magnet if necessary.

## K. HUMAN RESEARCH SUBJECTS

The appropriate IRB has jurisdiction in all experiments involving human subjects. General guidelines for human research studies in experimental protocols are:

1. All subjects will be evaluated by the attending physician, principal investigator, or designee, as to their physical and mental status before entering the KRCFBI.
2. All subjects will undergo screening for metallic objects before entering the KRCFBI, and those with critically implanted magnetic objects (i.e., aneurysm clips, pacemakers etc.) will not be allowed in restricted access areas of the KRCFBI.

3. No human experimentation will be performed without prior approval of the appropriate IRB and the KRCFBI/PRC .
4. All human subjects (or appropriate guardian) will sign an IRB-approved informed consent form before entering restricted access areas. A standard MRI subject screening form will be used; this signed document will be maintained with the signed IRB approved consent form.
5. In the event of an incident or medical emergency requiring medical attention to the human research subject, the operator shall remove the subject from the scan room, so that the emergency response team shall not need to enter the scan room.

#### L. ANIMALS

The appropriate Institutional Animal Care and Use Committee (IACUC) has jurisdiction in all experimental animal protocols. Kennedy Krieger Policies and Practices regarding Animal Experimentation shall be followed. General guidelines for animal experimentation in the KRCFBI are:

1. No animal experimentation will be performed without prior approval of the appropriate IACUC and the KRCFBI PRC.
2. All animals will sedated at all times during transport and when present in the KRCFBI. Furthermore, during transport through KKI all animals will be covered (e.g., by a sheet). Exceptions to the sedation requirement are possible for specific purposes (e.g., for functional MRI experiments), but they must be specifically requested in advance from the KRCFBI PRC.
3. No animals shall be transported through the KKI front lobby (near the elevators) All animals must be transported in and out of the center through the side door access to the KRCFBI. Prior arrangement must be made to obtain a key to this door.
4. All animals will be attended at all times while present in the KRCFBI.
5. A specially-designed animal holder ("cradle") is required for animal studies. Animals must be in this cradle at all times during transport through KKI and when present in the KRCFBI. The cradle shall be specifically designed to keep any animal detritus from soiling the patient bed, magnet bore, or any part of the center. Preferably catheters and diapers should be used to avoid contamination of the magnet table and bore. It is important to realize that any leakage of fluids (e.g. urine or blood) may go into the gradient unit and body coil (directly under the table) and cause electrical shortages and even fire! The animal holder, lines and catheters shall be designed without ferromagnetic parts and shall be inspected by center personnel to be approved for suitability with respect to cleanliness and safety.

6. No animals will be present in the KRCFBI during any procedure involving a human subject.
7. Animal studies will be performed after 5 p.m. or over the weekend to provide the opportunity for the ventilation system to dissipate any potential odors. Access rules and operator specifications shall be followed.
8. Researchers are responsible for thorough cleanup after animal experimentation. The scanner is primarily intended for human use and must be left completely clean and disinfected after use. Any violation may directly result (first offense) in withdrawal of the privilege to use the center.
9. Investigators using animals will be held responsible for the safety and cleanliness of their experiments; they will be required to agree in writing that their Department will pay for any loss of scanner time or instrument damage caused by error of the investigator.
10. Investigators using non-human primates are required to submit annually to the Center Safety Officer health reports on each individual potential subject. These health reports shall report serological titers of antibodies to the following viral agents: Herpesvirus simiae (B-virus), measles, simian immunodeficiency virus (SIV), simian retrovirus (SRV), and simian T-lymphotrophic virus-1 (STLV). In addition, the health reports shall report the result of an intradermal test for tuberculosis. The health report shall be submitted at least two weeks prior to the first anticipated visit by that animal to the Kirby Center, and the health data contained within the report shall pertain to tests performed on the animal no more than twelve months earlier.

## M. INCIDENTS

It is the duty of all operators to report all violations of safety procedure, all violations of protocols, all accidents, and any incidents requiring medical attention to human research subjects, to the KRCFBI safety officer immediately.

It is the duty of the KRCFBI safety officer to report all violations of safety procedure, all violations of protocols, all accidents, and any incidents requiring medical attention to human research subjects, to the KRCFBI Protocol Review Committee. The category of the incident is classified below:

1. Incidents in which any person was injured or received medical attention.
2. Incidents requiring the emergency quench of the magnet.
3. Incidents involving damage to KRCFBI equipment.
4. Conditions which constitute a safety hazard but are not covered by KRCFBI safety policy.
5. Incidents in which an approved protocol was not followed.

The safety officer is required to report incidents to the Director of the KRCFBI and to the Chair of the Protocol Review Committee or to the committee itself within the following time periods for the different categories:

1 and 2: To the Chair and the Director immediately.

3 and 4: To the Director immediately; to the Chair within 24 hours.

5: To the Director immediately; to the Protocol Review Committee at its next meeting.

The safety officer is also required to report incidents to the to the Office of Professional and Regulatory Affairs of the Kennedy Krieger Institute, via the Occurrence Report mechanism, as described in the Kennedy Krieger Institute Safety Policy and Procedure Manual.

#### N. GENERAL

1. At least one qualified Operator must be present when any MR system is being used.

Nothing in the foregoing is to be interpreted as preempting the legal and institutional responsibilities of the appropriate Institutional Review Board, IACUC, or such entities and agencies as have purview over safety and research procedures at KKI.