

**Guidelines for Ethics Approval of Research Protocols
Involving Human Exposure to Magnetic Resonance Imaging**

Required Wording in Informed Consent Documentation:

The Food & Drug Administration (USA) has indicated that for clinical diagnosis an 'insignificant' risk is associated with human MRI exposure at the intensities used in this project. Current Canadian guidelines follow the USA guidelines. Although very rare, injury and deaths have occurred in MRI units from unsecured metal objects being drawn at high speeds into the magnet or from internal body metal fragments of which the subject was unaware or had not informed MRI staff. To minimize this latter possibility it is essential that you complete a screening questionnaire. Other remote but potential risks involve tissue burns and temporary hearing loss from the loud noise inside the magnet. The latter can be avoided with ear headphone protection that also allows continuous communication between the subject and staff during the study.

MRI exclusion criteria

If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop or been a soldier, if you have some type of implanted electrical device (such as a cardiac pacemaker), if you have severe heart disease (including susceptibility to arrhythmias), if you are wearing metal braces on your teeth, or [for women] if you could be pregnant, or have an intrauterine device, you should not have an MRI scan.

A. Introduction:

The UWO Review Board for Health Sciences Research Involving Human Subjects frequently receives research applications that involved the use of healthy volunteers as imaging subjects. A review of Canadian MRI exposure guidelines raised some uncertainties re the safety of the exposure of control subjects to the magnetic fields. Since the potential benefits of this diagnostic tool are not directly applicable to healthy control participants as are the benefits to those experiencing disease symptoms of uncertain cause, concern surrounding the potential for harm to control participants becomes more relevant.

B. MRI Background:

MR Imaging, a widely used technology in modern clinical diagnosis, employs both a strong static and a time-varying 'switched' magnetic field as well as a rapidly oscillating radio frequency field (RF) to obtain tissue images in selected planes by virtue of the variable magnetic orientation and spin properties of the nuclei of different molecules. Although substantive evidence would suggest the magnetic fields to which humans have been exposed for such diagnostic purposes results in no serious harm, almost all such evidence to date has been based on study data in which field intensities were considerably lower than those now being produced by the current generation of imagers. More specifically, until recently the static magnetic fields involved in human imaging fell at or below 2 Tesla, while current imagers in London operate at field strengths ranging from 1.5 T up to 4 T (T = Tesla , the basic unit reflecting the intensity of the static magnetic field to which an object is exposed).

C. The Human Effects of MRI

Both theoretically and experimentally the **static** magnetic field effects appear to have a very high threshold of safety to human tissues, at least well above 4T. The lower intensity 'switched' magnetic field however, induces an electric field within the body that if of sufficient strength can cause peripheral nerve stimulation and therefore sensory or motor effects. If the switching rate or intensity of magnetic field is increased by a substantial factor above the peripheral nerve excitation threshold, stimulation of cardiac tissue is theoretically possible and this represents the greatest concern. For this reason, current international guidelines require that magnetic fields be kept at or below the peripheral nerve excitation thresholds and well below the cardiac stimulation thresholds. There is evidence as well that the 'switched' magnetic field at intensities below the nerve stimulation threshold can, in less than 5% of participants, elicit subtle and transient biologic effects such as nausea and dizziness. These effects have never been demonstrated to be detrimental and they have been minimized by moving the participant more slowly into the magnet.

The **radio frequency** field can increase local tissue temperature as well as body core temperature. It is relevant to note that outside the magnet's housing, the intensity of the magnetic field decreases rapidly with increasing distance, this decline being dependent in part on the size and design of the magnet and the diameter of its central bore. This information is of particular interest to MRI technical personnel working in this magnetic environment.

Despite these more theoretical risks, epidemiologic data gathered from extensive clinical imaging experience has not detected any significant deleterious effects of clinical MRI in the human to date other than those associated with metal implants as discussed below. The transient symptoms of nausea, dizziness and visual flashing lights that occur infrequently following exposure up to 4T are felt to be associated with changes in endolymph flow within the semicircular canals of the middle ear and retinal nerve stimulation respectively, but no lasting physiologic or pathologic effects have been noted to date. Similarly, animal exposure at these magnetic field intensities has shown only temporary behavioural changes that revert to normal as soon as they are removed from the field.

D. High Risk Groups

A well identified exposure risk is evident in individuals carrying metal implants such as cardiac pacemakers, joint prostheses, surgical /vascular clips, hearing aids and via previous metal-penetrating trauma that in some cases is unknown to the carrier. The ferromagnetism induced in these metal objects may cause movement of the implant that can result in injury to adjacent vital structures especially in the eye or brain or bleeding resulting from the torque on aneurysm clips. Electromagnetic disturbance of a cardiopacemaker's electronic program may lead to heart dysrhythmias. Special precautions for all individuals carrying such implants to minimize their risks of magnetic exposure during clinical imaging and otherwise their preclusion from the environment of an operating imager unless strongly indicated is emphasized in reputable MRI units. It is generally accepted that electric and magnetic fields should be considered separate entities that have distinct properties and effects on human tissues. However, since both

fields co-exist in MR imaging—i.e. the ‘switched’ gradients induce electric fields sufficient to trigger a nerve impulse-- it raises questions surrounding MRI exposure risks that might be analogous to the effects of magnetic fields induced by high tension electric power lines on human health. Despite the fact that the magnetic amplitudes surrounding high tension electric currents are approximately 1 million times less than those experienced in MR imaging, recurring evidence appears to link the prevalence of acute leukaemia in children with chronic environmental electromagnetic exposure during the first 2 years of life. This linkage does not persist when exposure is limited to the more mature childhood and adult years. Although the major difference in the chronicity of exposure from the electric power line field as compared to that associated with MRI should be emphasized, it would seem prudent to recognize infancy and early childhood (and possibly the fetal state) as a potentially more vulnerable age for exposure to induced electromagnetic energy in general.

In summary, from human studies of static magnetic field exposure up to 10 T and from clinical evidence involving well over 100 million clinical MRI scans, with the exception of those individuals carrying ferroimplants and possibly fetuses, infants and young children, there appears to be a substantial margin of safety with human exposure up to 4 T.

E. Historic Guidelines for Human MRI Exposure:

The US FDA first provided guidelines for MRI patient exposure in 1982 setting the ‘safe’ static magnetic threshold at 2 T adding further guidelines in 1988 to limit tissue heat induction and acoustic exposure. Harmonized guidelines were established by the EEC member states in 1994 basically incorporating the FDA recommendations. Revised FDA guidelines specifically designed for IRB’s were provided in 1997 and indicate an ‘insignificant risk’ for all age groups except neonates. The upper limit thresholds for the magnetic and acoustic components, (the latter because of the loud ‘bang’ related to the ‘switching’ of the magnetic field), are:

- a) **Static magnetic field:** 4.1 T
- b) **Specific Absorption Rate (SAR) of heat:** a limit of 4 watts / Kg /15 min whole body exposure or head exposure of 3 watts / Kg / 10 min.
- c) **time varying ‘switched’ field:** case by case limit to avoid severe discomfort or painful nerve stimulation
- d) **Acoustic peak sound pressure limits:** 140 decibels (dB) or 99 dB with hearing protectors.

F. Current Canadian Guidelines:

The Health Protection Branch of the then Department of National Health and Welfare of Canada published ‘Guidelines on Exposure to Electromagnetic Fields from Magnetic Resonance Clinical Systems’ in 1987. It was stated that their exposure guidelines reflected ‘minimal, if any, health hazard’,--- and that ‘exceeding the limits specified are not necessarily hazardous, but a careful individual evaluation should be done as the presently available scientific data are not sufficient for providing general recommendations.’

Although now considered outdated, the Canadian guidelines are provided to illustrate the rate at which this technology is evolving.

1. Under the '**Patient**' category, exposure limits are:
 - a) static magnetic field: 2 T.
 - b) time-varying magnetic fields: 3T/sec
 - c) RF magnetic field: which does not cause an increase of body temperature (core or rectal) of more than 0.5C and of any part of the body of more than 1C.
2. Under the '**Operator**' category:

'Operators of MRI devices should not be continuously exposed to a magnetic flux density exceeding 0.01 T during the working day. Exposures to higher flux densities are permitted for short-time durations (about 10 min per hour); their number and duration should be minimized.'
3. **Special considerations:**

Individual assessment of suitability for MRI and precautionary measures should be employed for pregnant women, those wearing cardiac pacemakers and those bearing metallic implants (tooth fillings are not considered a hazard).

G. REB Considerations:

Until more current guidelines are provided by Health Canada or other national regulatory Agencies, the UWO REB will consider the following items when reviewing applications involving MRI research protocols:

1. Assurance that upper magnetic exposure limits as defined in the 1997 US FDA Guidelines noted above (or most current at the time) be recognized and respected by the applicants.
2. All individuals who are to be subjected to magnetic fields greater than the limits specified in # 1, should be specifically informed through a signed consent that although to date there is no substantive evidence of significant harm at the planned intensities, there are still insufficient numbers of well designed, controlled human studies available to demonstrate the absolute safety of the MRI protocol being considered.
3. Control MRI participants in particular should be knowledgeable about the principles of magnetic fields and MRI technology, its known effects on human tissue, its potential to cause harm even though this has not been demonstrated to date, and the availability of current guidelines for human MRI exposure. Precautions should be taken to ensure there is no overt or tacit inducements to specifically recruit trainees or technical staff working in the MRI laboratory under the supervision of professional staff as 'control' participants beyond their voluntary response to a general advertisement.
4. Special precautions should be taken to ensure both potential MRI study and control

participants who might be carrying unrecognized metal implants or an early pregnancy are identified and individually assessed as candidates before study exposure. It is difficult to justify the MRI exposure of pregnant individuals, infants and children as control participants until data documenting the absence of longer term health risks to these groups becomes available.

Reference Sources:

1. 'Guidelines on Exposure to Electromagnetic Fields from magnetic Resonance Clinical Systems', Environmental Health Directorate, Health Protection Branch, Department of National Health and Welfare Canada, 1987.
2. 'Magnetic Resonance Imaging', Clinics of North America, 6: (Nov), 1998.

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Sample Informed Consent Language: Magnetic Resonance Imaging (MRI)

If your protocol involves Magnetic Resonance Imaging (MRI), special consideration of this fact must be included in the consent form. The following provides some suggestions for wording in the Letter of Information and Consent documentation.

This MRI machine uses a strong magnet and radiowaves to make images of the body interior. The scanning procedure is very much like an x-ray CT scan. You will be asked to lie on a long narrow couch for a certain amount of time [state how long] while the machine gathers data. During this time you will not be exposed to x-rays, but rather a magnetic field and radiowaves. You will not feel either. You will, however, hear repetitive tapping noises that arise from the radio antenna around your body. We will provide earplugs or ear phones that you will be required to wear. The space within the large magnet in which you lie is somewhat confined, although we have taken many steps to relieve the "claustrophobic" feeling.

There are no known significant risks with this procedure at this time because the radiowaves and magnetic fields, at the strengths used, are thought to be without harm. The exception is if you have a cardiac pacemaker, or a certain type of metallic clip in your body (i.e., an aneurysm clip in your brain). There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is not unexpected and should not be painful. However, you can discontinue the exam at anytime.

The magnetism and radiowaves do not cause harmful effects at the levels used in the MRI machine. However, because the MR scanner uses a very strong magnet that will attract metal, all metallic objects must be removed from your person before you approach the scanner. In addition, watches and credit cards should also be removed as these could be damaged. (These items will be watched for you).

RISKS

If you have any history of head or eye injury involving metal fragments, if you have ever worked in a metal shop or been a soldier, if you have some type of implanted electrical device (such as a cardiac pacemaker), if you have severe heart disease (including susceptibility to arrhythmias), if you are wearing metal braces on your teeth, or [for women] if you could be pregnant, you should not have an MR scan.

If you wish, we can prescribe a mild sedative to help you to relax during the scan session. Because you may still feel sleepy after taking this medication, you should not plan on driving yourself after the MRI.

NOTE: IF ALL OF THE SEQUENCING TO BE USED HAS NOT BEEN APPROVED BY HEALTH CANADA, THIS MUST BE STATED IN THE INFORMATION / CONSENT DOCUMENTATION.