Western Research

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Guidance Document	Magnetic Resonance Imaging
Effective Review	Delegated & Full Board
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A. Preamble

Western has been a Canadian leader in the use of MRI for research purposes for over 25 years. Guidance documents developed to aid the Health Sciences Research Ethics Board (HSREB) in evaluating research proposals have become dated and do not reflect current regulatory practice. This document is generated to bring the HSREB Guidance documents into alignment with modern best practices.

B. Introduction

The HSREB at Western University frequently receives research applications that involve the use of (1) healthy adult participants volunteering for magnetic resonance imaging (MRI) studies, (2) healthy minors (adolescent, pediatric or neonatal) volunteering to participate in MRI studies, or (3) patients in all age groups participating in MRI studies beyond what would be considered medically necessary for their care. While MRI is used routinely for diagnostic imaging, the potential benefits of a diagnostic procedure are not applicable for many of the HSREB submissions. Thus any potential risks to the participants needs to be assessed.

MRI is a complex technology, with many possible confusing variations and constraints governing its operation. The goal of this document is to (1) explain these variations, (2) describe the regulatory environment, (3) provide the current best practice for risk or safety assessment when normal operating limits are exceeded, (4) provide clear guidance to the HSREB as to the level of review needed under different MRI operating conditions and (5) provide guidance to scientists who may submit protocols for REB review.

C. Magnetic Resonance Imaging and Spectroscopy (MRI/MRS)

MRI is a widely used imaging modality for both clinical diagnosis and investigational research in humans and animal models because of its capability to evaluate anatomic, physiologic and functional information in a (usually) non-invasive manner. There are approximately 25,750 MRI systems in operation world wide, performing 54 million procedures annually. About 2000 new scanners are delivered on an annual basis worldwide. According to the 2014 OECD report, MRI exams in G7 countries average 51 (range 40-106) exams per 1000 population per year (http://dx.doi.org/10.1787/mri-exam-total-table-2014-1-en). In the US, effectively 10% of the population receives an MRI every year (32 million MRIs are performed annually in the country). About 1.5 million MRI procedures are conducted in Canada on an annual basis on 265 scanners (as of 2014).

MRI does not use ionizing radiation, and therefore does not carry the risks associated with x-ray procedures. This has contributed to its popularity in both diagnosis and research applications, where it can be used freely for longitudinal studies. However, it is important to understand how an MRI scanner operates in order to assess any safety concerns and any risks associated with the

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technology and understand the regulatory framework.

In MRI, three different electromagnetic fields are employed to create tissue specific information and contrast. These are, **(i)** a strong static magnetic field, **(ii)** a radiofrequency field, and **(iii)** time-varying magnetic field gradients. In addition to the three electromagnetic fields, **(iv)** the acoustic sound pressure levels in the MRI scanner must also be considered. This too will be reviewed below.

There is a vast literature investigating the electromagnetic fields produced by MRI systems and their subsequent effects on the human body. This literature has been used by regulatory agencies to develop safety recommendations. Because these have been extensively examined by expert panels and various regulatory agencies, they are not individually reviewed here. *The important point to note is that MRI scanners operating within regulatory agency-defined limits and appropriate safety practice guidelines are considered non-significant risk by these agencies.* Operating outside of those limits requires informed consideration by ethics review boards as well as informed consent of the participant.

MRI studies sometimes use contrast agents (classified as drugs by the (U.S. Food and Drug Administration (FDA) and Health Canada) that are injected intra-vascularly to improve delineation of tissues (e.g. imaging arteries) or are injected or inhaled as molecular agents such as iron oxides or Helium or Xenon. The most common contrast agent (chelated Gadolinium) is generally safe. In patients with normal kidney function gadolinium contrast medium that is injected is almost entirely passed out in the urine within 24 hours. Gadolinium contrast medium should be avoided in patients with reduced kidney function or kidney failure (acute or chronic) and hepatorenal syndrome (a condition involving reduced function of liver and kidneys). Nephrogenic systemic fibrosis (NSF), a debilitating disease resulting in skin contractures (or localized skin thickening and tightening) and internal organ damage or death has occurred with some gadolinium based contrast agents in a minority of patients who had pre-existing severe kidney function abnormalities.
The most common adverse reactions of gadolinium are headache, nausea and dizziness for a brief time following the injection. This occurs in 1% to 5% of contrast injections. Infrequently, a feeling of coldness may occur at the injection site.

Allergic (anaphylactic) reactions to gadolinium contrast medium have occurred but are extremely rare, occurring in about 1 in 10,000 people. Such reactions, which may involve breathing or swelling of the lips and mouth, fortunately respond very well to emergency drug treatment in almost all cases.

In conclusion, because the risks associated with contrast agents (particulate, liquid or gaseous) are generally higher than those encountered in participants' daily lives, MRI utilizing them cannot be considered a non-significant risk, and should be scrutinized by full board review.

D. Regulatory environment

Regulatory agencies have set limits on the four major operating parameters of MRI scanners discussed above (**(i)** to **(iv)**) since the very inception of MRI as a diagnostic and research tool. Static magnetic fields have increased 100 fold since the first MRI demonstrations, supported by a large number of studies that examine biological effects. In London (and in Canada), there are no human scanners operating above 7T and none planned. There are currently sixty 7T scanners

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operating worldwide, one 8T and a handful of 9.4T, 10.5T and 11.74T scanners as well. Scanners above 8T operate with an Investigational Testing Authorization or equivalent and require local IRB/HSREB approval for every study. Scanners operating at 8T and below are deemed non-significant risk, subject to certain operating constraints. Siemens applied to the FDA for 510(k) marketing approval for 7T as a diagnostic tool in May 2015, being the first major vendor to do so. The limit of 8T is based on the fact that there has been 19 years of experience with fields up to this value, thousands of patients scanned and many safety studies performed. The paucity of scanners operating above this has meant that insufficient time has passed in order to accrue a safety profile at this time.

The evaluation of MRI studies conducted at Western should be tied to FDA and Health Canada standards and should be compliance with NIH and Tri-council policies. This is the framework that the HSREB operates and under which it is certified. These regulatory standards are presented below.

(1) United States Food and Drug Agency (FDA).

Magnetic resonance diagnostic devices are Class II devices described under 21 CFR 892.1000. When operated within the guidelines described in **(i)** to **(iv)** below, MRI instruments are determined to have non-significant risk. That is, they operate with a risk profile similar to menstrual pads, band aids, daily wear contact lenses, digital mammograms and insulin monitors. The 2014 FDA guidance for non-significant risk MRI studies is presented in http://www.fda.gov/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm072686.htm and in http://www.fda.gov/RegulatoryInformation/Guidances/ucm073817.htm

The current FDA guidelines for MRI have been in place since 2003. With respect to the 4 criteria listed in **B(i)** to **B(iv)** below, the following operating constraints must in place for scanner operation to be considered a non-significant risk.

(i) **Static magnetic field:** MRI studies involving static fields of 8T and below pose non-significant risk to participants 1 month and older. A static field limit of 4T has been imposed for infants below 1 month of age.

(ii) **Radiofrequency fields:** With respect to Specific Absorption Ratio (SAR) which is linked to heating by the radiofrequency field, whole body SAR limits are limited to less than 4 W/kg (Watts per kilogram) for any 15 minute average and whole head SAR limits are set to less than 3.2 W/kg for any 10 minute average.

(iii) **Time-varying magnetic field gradients:** The FDA restricts the rate of change of the magnetic field gradients to less than a value that would produce severe discomfort or painful nerve stimulation.

(iv) **Sound Pressure Level:** The peak un-weighted sound pressure level must not exceed 140 dB and the A-weighted root mean square sound pressure level must not exceed 99 dBA when hearing protection is worn.

MRI scanners operating in London operate in Normal mode or First level controlled mode. The normal operating mode is considered safe for all patients, regardless of their condition. The first level controlled mode is defined as one in which operating parameters (dB/dt or SAR) reach values that may cause physiological stress, and the Second level controlled mode is one in which parameters reach values that may produce significant risks for patients. The FDA mandates that human studies protocol for operation in the Second level controlled mode be reviewed by a

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Research Ethics Board.

Prior to this guidance, the FDA had issued marketing approvals based on the IEC (European) operating mode scheme, but had not specifically recommended this feature. However, since MR equipment is a worldwide market, all manufacturers currently market scanners that conform to the IEC requirements. With the adoption of this guidance, FDA began recommending utilization of the IEC operating mode scheme.

As mentioned, all commercial MRI scanners operate in Normal mode or Level one controlled mode. Any scanning performed under second level controlled mode requires a full-board HSREB review detailing the particular risks associated with the parameter(s) that exceed the FDA guidelines and there needs to be an appropriate letter of consent for the participant.

(2) Health Canada (HC).

In 1987, 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". At the time, 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." These guidelines are now considered to be severely outdated and are superseded by newer guidance from revamped agencies.

These days, Health Canada regulates the importation and sale of medical devices and radiation emitting devices in Canada through the *Food and Drugs Act*, the *Radiation Emitting Devices Act*, and the *Medical Devices Regulations*. Additional regulations limiting SAR come from Industry Canada's guidelines. While the SAR guidelines were developed for cellular phone radiofrequency operation, they apply equally well to MRI systems. MRI devices are evaluated by Health Canada's Therapeutic Products Directorate (TPD) as Class II (same as the FDA). Class II devices are considered low-risk, and include items such as surgical gloves, daily wear contact lenses, dentures and condoms http://www.hc-sc.gc.ca/dhp-mps/md-im/applic-demande/guide-ld/gd_rbc_non_ivdd_lg_scr_autres_idiv-eng.php. For reference, a mammography or CT system or extended wear contact lenses are Class III, i.e. moderate risk. A toothbrush is Class I. MRI RF coils, are also classified as Class II because devices attached to a Class II device are expected to be controlled and monitored by the Class II device. Health Canada's TPD does not set limits on any of the MRI operating parameters **(i)** to **(iv)** discussed above in the FDA section, but does implicitly follow the FDA guidelines given that all FDA approved MRI scanners have also obtained Health Canada approval. In some cases, such as the Siemens Magnetom Prisma at the Robarts Research Institute, Health Canada led the licensing approval http://webprod5.hc-sc.gc.ca/mdll-limh/information.do?deviceId_idInstrument=592358&deviceName_nomInstrument=MAGNETOM+PRISMA&licenceId=91783&lang=eng.

Overall, both the FDA and Health Canada consider the risks associated with MRI use comparable to many common health care devices such as daily wear contact lenses. In the FDA vernacular, MRI is considered "non-significant risk". In Health Canada's verbiage, MRI is considered "low-risk". Both NIH and Tri-Council policy recommend delegated review of this risk level under the concept of proportionate review. If an IRB or HSREB makes a different judgement regarding risk (for MRI or anything else deemed low risk), they are obligated to notify the FDA and Health Canada of their reasons. Not doing so constitutes withholding of information from the

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regulator and is punishable by large fines and jail time.

(3) Province of Ontario.

The Province of Ontario has been proactive in ensuring MRI facilities are safe from a design and operational standpoint. Their comprehensive document produced in 2007 can be found at http://www.health.gov.on.ca/en/common/ministry/publications/reports/disc_ct_mri/mri_report.pdf. This document provides no guidance on the 4 FDA MRI operating criteria, but lays out policies and procedures for staff and patients working around MRI systems, for safety zones from Level I to Level IV. These recommendations are followed by all commercial MRI systems operating on the Western campus. The Ontario document follows recommendations from an earlier version of the American College of Radiology White paper on MRI safety. The latest version of that White Paper (2013) can be found here http://www.acr.org/Quality-Safety/eNews/Issue-02-June-2013/MR-Safety-Report.
The Canadian Association of Radiologists have also endorsed this document http://www.car.ca/uploads/standards%20guidelines/20110428_en_standard_magnetic_resonance.pdf. While these documents do not provide guidance on MRI operating parameters, they do address the major risks associated with MRI, which derive from accidents, not the procedure itself. As such, they form excellent best practice guidelines. These guidelines have been implemented in the MRI suites at Robarts Research Institute, Lawson Health Research Institute and at the hospitals.

E. What happens when FDA limits are exceeded?

As noted, regulatory agencies have set limits on the four major operating parameters of MRI scanners discussed above (**(i)** to **(iv)**) since the very inception of MRI as a diagnostic and research tool. When operating within the FDA limits, MRI is considered a non-significant risk Class II device by the FDA and a low-risk Class II device by Health Canada. In order for the HSREB to make an informed decision about studies that might exceed the guidelines, some background on safety and bio-effects is provided below.

(i) Static magnetic field

The magnetic field is used to polarize the spins in the body, conferring a weak magnetism to the tissue. This affects approximately one in a million spins and thus does not "magnetize" the body in the sense we are accustomed to (e.g. a fridge magnet). The higher the static magnetic field, the higher the spin polarization, which leads to a higher MRI signal. This is the main motivation for higher magnetic fields in MRI. The currently established guidelines for static magnetic field are 8 Tesla (T) for adults, children and infants more than one month old. Through an abundance of caution (no adverse affects have been recorded), the limit for infants one month or younger has been restricted to 4T. A Tesla (T) is the metric unit of magnetic field strength. One Tesla is approximately 20,000 times the earth's magnetic field.

These guidelines, informed by a (lack of) bio-effects, have been arrived at through 4 decades of studies or assessments performed by numerous regulatory and health agencies including the WHO, the FDA, the ICNIRPF, Health Canada, the IEC, the EC, the AAPM and others. The most recent summary can be found in a publication from the International Commission on Non-Ionizing Radiation Protection (ICNIRPF) in the journal Health Physics (106(3):418-425; 2014).

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While the static magnetic field up to the current regulatory guidelines is considered safe from a biological perspective, the primary risk to a participant arises from the effect of the MRI magnet on ferromagnetic materials in the environment (e.g. compressed gas cylinders, scissors), as well as mechanical (e.g. aneurysm clips, orthopaedic implants, metallic fragments) and electronic (pacemakers, cochlear implants) implanted devices. The potential hazard of the projectile effect of ferromagnetic material in a strong magnetic field is a serious concern in MR units. This risk can be minimized by the strict and careful management of the MR unit as specified in the American College of Radiology Guidance Documents for Safe MR Practices: 2013 (http://www.acr.org/Quality-Safety/eNews/Issue-02-June-2013/MR-Safety-Report and www.health.gov.on.ca/en/common/ministry/publications/reports/disc_ct_mri/mri_report.pdf) and through a rigorous participant screening procedure, such as the verbal and written forms adopted by Western and other institutions (available on the HSREB web site).

In summary, the main MRI risks associated with the magnetic field are related to projectiles, mechanical and electronic implants as discussed above. The actual risk of death through these latter mechanisms has been reported as 4 per 100 million MRI scans, comparable to driving 16 km in an adult-driven car and ten-fold lower than driving 16 km with a teenager at the wheel. The MRI risk of death actually decreases with field. There are no known deaths attributed to scanners operating at 4T and above, likely because these are in high-end academic centres with substantial oversight.

For the foreseeable future, all Canadian MRI studies operate within the FDA non-significant risk limits for magnetic field strength. Thus additional information is not provided on the theoretical bio-effects of static magnetic fields, as the HSREB will not need to assess the risks for operation above the regulatory limits. It is possible that an investigator may wish to scan infants below one month at the highest available field strength in London (and Canada) (7T), which would require operation outside of the regulatory limits. If such a case arises, the submission to the HSREB should include a full review of the literature available, rather than relying on a brief summary here.

(ii) Radio-Frequency (RF) fields

The RF fields produced in the MRI scanner are designed to "excite" the spin polarization described above in **(i)**. As the excited spins return to their initial polarization, they give off a very weak RF signal that is exploited by MRI receiver coils to generate the contrast in MRI images. The rate of deposition of RF energy used for excitation is measured in Watts per kilogram (W/kg). This is termed the Specific Absorption Rate. The FDA guidance for SAR depends on the organ being imaged. In the head, the non-significant risk limit is less than 3.2 W/kg averaged over a 10-minute period. In the body, the non-significant risk FDA guidance allows up to 4 W/kg over any 15-minute period. Additionally, in the head or torso, no gram of tissue may exceed 8 W/kg over 5 minutes, and in the extremities, no gram of tissue may exceed 12 W/kg over 5 minutes.

The rationale for these limits come from the fact that core body temperatures can rise many times this amount during normal exercise, and therefore the body clearly has mechanisms to be able to cope with this type of increase. For reference, the human brain generates approximately 10W/kg of heat at rest. The reduced limits in the head are driven by providing a margin for protection of the lenses of the eyes, which are not perfused and are therefore limited in their ability to dissipate heat. Specific guidelines are mandated on all clinical systems to keep tissue heating below the 1 degree Celsius limit while operating in Normal mode (see below). The SAR limits are set by agencies such as the US FDA, the International Electrotechnical Commission and Industry Canada. In particular, these limits also apply to cellular telephone usage and are backed by large

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scale epidemiological studies in adults and children by manufacturers and public health agencies.

As with static fields, the concern with bio-effects when operating within the above-mentioned regulatory limits is unwarranted. However, other safety considerations do apply, just as they do with magnetic fields. The main safety issues for the RF fields used in MR are thermal heating leading to heat stress, induced current burns and contact burns.

Absorption of energy from radiofrequency fields used in MR results in the increased oscillation of molecules and the generation of heat. If this occurs in human tissue, a compensatory dilation of blood vessels results in an increase in blood flow and the removal of the excess heat, which is dissipated mainly through the skin. Heat stress is of particular concern for some patients, such as those suffering from hypertension, pregnant women, or those on drugs such as diuretics or vasodilators that may compromise these responses. One fundamental issue is excessive cardiovascular strain resulting from thermoregulatory responses to body temperatures raised over a short period of time by more than 0.5°C in vulnerable people.

The RF field can induce currents in conductors and can raise their temperature significantly. Burns to volunteers and patients from contact with such metallic objects can be avoided by careful positioning and set up within the bore of the magnet. Examples of such causes are: contact with metal in clothing, RF coils, RF coil leads, ECG connectors and oxygen monitor probes. These burns can occur even in a MRI scanner operating within regulatory guidelines and can only be avoided through careful MR unit operation by knowledgeable MRI staff.

Certain types of makeup and tattoos (containing iron pigments), piercings etc. can lead to localized burns as well. These can occur regardless of the scanner operating within regulatory limits. These can only be alleviated by careful verbal and written screening forms, observation by the MRI technologist and awareness by the subject to report any sensations prior to reaching a pain threshold.

RF burns are the major contributor to the 17 per 100,000 incidence of injury while undergoing an MRI and are avoidable with careful safety practices, subject honesty (e.g. about a piercing or tattoo) and staff training. Comparing the 17 in 100,000 incidence above, the risk of injury for children under the age of 16 ranges from 300-750 per 100,000 hours of participation in soccer and 12,730 per 100,000 hours of playing ice hockey. Also for reference, a typical MRI lasts 1 hour, thus the risks can be equated on an hourly basis. Statistics Canada reports that an estimated 4.27 million Canadians aged 12 or older suffered an injury severe enough to limit their usual activities in 2009–2010 (http://www.statcan.gc.ca/pub/82-624-x/2011001/article/11506-eng.htm). This represents 15% of the population in that age range on an ongoing basis. Thus it can be seen for SAR (and MRI in general), the risks of injury are enormously below those for participation in daily activities for both children and adults.

In summary, RF electromagnetic fields delivered within the regulatory agency guidelines are considered a non-significant risk. Levels beyond these require REB review,deliberation and informed consent. For scanners operating within the regulatory limits, minor burns are still possible. These can be avoided by screening the subjects for the known safety contraindications described above and through the use of experienced MRI personnel.

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(iii) & (iv) Time varying magnetic field gradients

MRI scanners use a component called a gradient coil to perform spatial encoding of the MRI signal and allow reconstruction of an image. This gradient coil is driven by three powerful amplifiers (100,000 W compared to the typical 500 W home audio amplifier). The regulatory agencies set limits on how fast these magnetic fields can oscillate and how loud a noise the gradient coil can produce (since it functions very much like a loudspeaker). The rate of switching is first discussed, followed by the sound pressure levels.

Magnetic field gradients in commercial systems operate as high as 80 mT/m (milliTesla per meter) and can change at 400 mT/m/ms. The safety concerns with the time-varying magnetic field gradients are biological effects (i.e. peripheral nerve stimulation and muscle stimulation) and acoustic noise.

Subjecting the human body to time-varying electromagnetic fields can lead to induced electric fields and circulating currents in conductive tissues. At any particular location, the currents induced will be determined by the rate of change of the magnetic field and the local distribution of the body impedance. Time-varying magnetic fields induce electric currents that potentially interfere with the normal function of nerve cells and muscle fibres. An example of this is peripheral nerve stimulation (PNS). A more serious response to electric currents flowing through the body is that of ventricular fibrillation.

At low frequencies, induced currents are able to produce the effect of stimulation of nerve and muscle cells. The extent of stimulation will depend on the pulse shape and its repetition rate. This stimulation can be sufficient to cause discomfort and in extreme cases might result in limb movement or ventricular fibrillation. The body is most sensitive to fibrillation at frequencies of between about 10 Hz and 100 Hz and to peripheral nerve stimulation at up to about 5 kHz – precisely the range that gradient coils operate. Above these frequencies, nerve and muscle cells become progressively less responsive to electrical stimulation.

Clinical scanners operating within IEC or FDA limits will not produce the PNS or cardiac effects noted above and thus operate at non-significant risk. There are conditions where a subject may report a tingling sensation in the nose or toes depending on the type of MR imaging sequence being performed. The subject is unlikely to be alarmed if they were instructed to be aware of the possibility of such events. The list of cardiac fibrillation due to switched field gradients is based on theory rather than actual adverse events. There has never been a report of cardiac fibrillation caused by an MRI scanner.

As mentioned, the rapidly switched currents passing through the gradient coil mimic the operating principle of a loudspeaker. As such, the vibrations of the gradient coil can create loud buzzing/banging noises that can cause temporary hearing impairment if experienced over time frames that are typical of an MRI scan. In Normal and Level one controlled mode, sound pressure levels that can cause damage are forbidden. An MRI scanner is said to operate with non-significant risk with regard to the time varying magnetic field criteria if (1) a peak unweighted sound pressure level less than 140 dB (decibel) is maintained, and (2) an A-weighted root mean square (rms) sound pressure level less than 99 dBA is maintained with hearing protection in place. For reference, a trumpet at 1 m has a SPL (sound pressure level) of 130 dB. Traffic on a busy roadway 10 m away averages 80-90 dB. The risk is alleviated by using hearing protection (i.e. ear plugs) and/or MRI compatible headphones.

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In summary, the potential bio-effects of MRI scanners operating within FDA guidelines for gradient coil performance are confined to nuisance sensations. No adverse events have been reported. An MRI scanner is said to operate with non-significant risk with regard to the time varying magnetic field criteria if any time rate of change of gradient fields (dB/dt) sufficient to produce severe discomfort or painful nerve stimulation is avoided. If a scanner operates outside of these limits, then fully considered HSREB review is merited and the operating condition must be disclosed in the letter of consent.

F. Special considerations for children

Numerous past and ongoing studies utilize children in MRI studies of development. Most of these studies are in fact longitudinal, with many MRIs performed over the course of the study. There are major consortia utilizing MRI to study healthy brain development, including the human connectome project http://www.nimh.nih.gov/funding/grant-writing-and-application-process/concept-clearances/2014/lifespan-human-connectome-project-children-and-adolescents.shtml and the preterm development project https://www.ucl.ac.uk/preterm-development-project/what/mri. An outstanding review of the safety and risk profile for scanning pediatric populations is provided here http://www.mrineonatalbrain.com. These, and hundreds of previous studies are allowed to proceed on the demonstrated basis of non-significant risk to the participant. The exception to non-significant risk comes from the use of sedation in some pediatric studies.

The FDA guidelines distinguish between adults and children in only one criterion, that of the static magnetic field. Through an abundance of caution, magnetic field strengths of 4T have been set as the upper guidance limit for infants below the age of one month. Health Canada does not explicitly distinguish between adults, children and infants for MRI. Industry Canada makes no distinction for SAR limits based on age or sex with respect to cellular phones. It should be noted that SAR is measured in W/kg and therefore implicitly accounts for body size. A recent Canadian survey of the safety literature and relative risks determined that MRI in pediatric populations posed non-significant risk, with the proviso that neither sedation or contrast agents were used http://www.thehastingscenter.org/Publications/IRB/Detail.aspx?id=5516. This publication also noted that the stress and anxiety associated with an MRI was actually less than what children reported in standardized neuropsychological evaluations of their daily life. It is important to note that sedation per se is not a risk associated with MRI, but any study proposing to use sedation should be subject to full board scrutiny.

G. HSREB Guidance

Based on the review of the regulatory framework concerning MRI above, and the ethics guidance provided by NIH and the Tri-Councils for proportionate review of low-risk studies, the following guidance for Western's HSREB are provided.

1. For MRI studies that are conducted under the non-significant risk FDA guidelines for adults and children, the HSREB should utilize delegated review.

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2. For MRI studies conducted in the FDA/IEC Level II controlled mode (i.e. those that exceed the FDA non-significant guidelines or bypass FDA mandated safety systems), full board approval should be sought.
3. For MRI studies conducted in the FDA/IEC Level II controlled mode (i.e. those that exceed the FDA non-significant guidelines or bypass FDA mandated safety systems), explicit mention of the limits being exceeded and the implication thereof should be provided in the letter of consent.
4. Any MRI study that requires the use of contrast agent or sedation should also be evaluated by the full board.
5. Any MRI study performed on an experimental system (i.e. not provided by a clinical vendor) should be evaluated by the full board to ensure that FDA limits are being respected.
6. Any MRI study performed on an experimental system (i.e. not provided by a clinical vendor) should explicitly mention the experimental status of the system in the scientific proposal and HSREB submission and in the letter of consent.

Subject to these conditions, the HSREB should consider MRI studies for adults, children and infants for delegated review, unless other criteria which may cause physical or mental anguish are also part of the study (e.g. pain studies, evocation of previous trauma).

Risks of MRI (Magnetic Resonance Imaging) Scans (to be included in the consent form)

There are no known biological risks associated with MR imaging. Some people cannot have an MRI because they have some type of metal in their body. For instance, if you have a heart pacemaker, artificial heart valves, metal implants such as metal ear implants, bullet pieces, chemotherapy or insulin pumps or any other metal such as metal clips or rings, they cannot have an MRI. During this test, you will lie in a small closed area inside a large magnetic tube. Some people may get scared or anxious in small places (claustrophobic). An MRI may also cause possible anxiety for people due to the loud banging made by the machine and the confined space of the testing area. You will be given either ear plugs or specially designed headphones to help reduce the noise.