MRI STANDARD SAFETY PROTOCOLS AND ETHICAL CONSIDERATIONS

FINAL REPORT

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Montreal, March 2016

In March 2015 I arrived at McGill University as a visiting professor under the supervision of Dr. Rick Hoge and Dr. Sylvain Baillet at the McConnell Brain Imaging Centre. The main focus of my project was to develop an MRI safety manual with a set of standard operation protocols (SOPs) and appropriate ethical guidelines for conducting research in the Republic of Macedonia. This manual is the first of its kind in the Republic of Macedonia, and is a crucial step in the establishment of the Macedonian MRI research center that is intended to be a cutting-edge institution that can accommodate a wide range of research and clinical activities.

This project continues the previously established clinical and academic collaboration between experts from the Montreal Neurological Institute - McConnell Brain Imaging Centre, and researchers from the Republic of Macedonia in the field of medical imaging. As part of this collaboration, Macedonian professionals and trainees have been visiting the McConnell Brain Imaging Centre as observers since 2013, and they are currently involved in implementing novel clinical and research protocols on the imaging equipment recently purchased by the Macedonian Ministry of Health. Keeping in mind that standardized screening and safety procedures for research participants, patients and imaging professionals operating the equipment are key elements in the successful operations of an imaging center, the McConnell Brain Imaging Centre welcomed me to investigate the ethical, occupational, and public health aspects of MRI.

During this process, I was faced with the challenge and responsibility to create a safety training course syllabus for MRI staff in an interdisciplinary and multicultural environment, with particular emphasis on occupational health standards and practices. The first part of my appointment consisted of site visits at three MRI research facilities located in Montreal. In addition to the 1.5T and 3T research MRI scanners at the McConnell Brain Imaging Center, I also spent time at two MRI research sites at the University of Montreal (UdeM): the Montreal Heart Institute, and the Geriatric Institute Functional Neuroimaging Unit. Following a period of familiarization with MRI equipment and standards, in August 2015 I established a close collaboration with academics and professors at the Department for Epidemiology, Biostatistics, and Occupational Health (EBOH), who helped me develop a syllabus for an Occupational Safety Training course targeting MRI professionals. The letter of acceptance with description of my research activities is attached to this report.

As visiting professor at EBOH,I had access to a wide range of resources, including an office, computer, and the course materials and lectures offered by EBOH. As part of my research, I developed a close collaboration with the Environmental and Occupational safety Department, which is responsible for all mandatory safety-training activities at McGill University. I also had the opportunity to participate as an auditor and guest lecturer in several Occupational Health and Occupational Safety Practices courses, as well as the courses for Workplace Physical and Biological Hazards, Burden of Diseases and Environmental Health Science. This allowed me to work on the development of course materials on topics that are not included in the occupational safety and health education program in the Republic of Macedonia. My special interest was to develop a course syllabus for Occupational Safety Practices and Occupational Health Practices.

My report is structured in three parts:

I. MRI Safety Guidelines
II. MRI Research Ethical Standards
III. MRI Occupational Safety Training Course Syllabus

Each part contains an explanation of the current situation in Macedonia and proposals for future activities aiming to develop modern and internationally recognized MRI safety procedure and ethics standards.

I. MRI safety Guidelines

Magnetic resonance imaging (MRI) is a cross-sectional imaging technique that uses a large magnetic field, rapidly fluctuating orthogonal magnetic field gradients, and electromagnetic radiation in the form of radio waves. All magnetic resonance devices (MRD) in use in Macedonia are at field strength of 1,5 T or lower. Currently, there are no research dedicated MRI scanners.

The National MRI Safety Guidelines should address many different safety aspects from legislation to the practices for labeling, screening, fire protection/quench and many others. These safety guidelines should require all MRI units to develop their own MRI Safety Manual. Below are the most important issues that need to be addressed.

1. Basic prerequisites

1.1. Legislation

Many Universities, research centers and MRI facilities have developed their own MRI safety manuals. All of them are based on the federal and provincial guidance documents concerning the safe operation of equipment generating significant magnetic and electromagnetic fields, as described in the Canadian Guidelines on Exposure to Electromagnetic Fields from Magnetic Resonance Clinical Systems (Safety Code 26 – http://www.hc-sc.gc.ca/ewh-semt/pubs/radiation/87ehd-dhm127/index-eng.php).

In the Republic of Macedonia there is a rule book for workplace risk assessment of the workers exposed to electromagnetic fields. Unfortunately, this document is harmonized with EU Directive 2004/40/EC which wasn't compatible with working in MRI environment. Because of this, Directive 2004/40/EC was repealed by a new directive 2013/35/EU. The new Directive proposes exposure limit values (ELV) and actions levels (ALs) in the frequency range from 0 Hz to 10 MHz that are compatible with the MRI operational practices, and the safety of the staff, patients and research participants.

Proposal 1: Propose to the Ministry of Work and Social Policy and Ministry of Health to repeal the actual by-law and acceptance of a new by-law document/rulebooks for workplace risk assessment of the workers exposed to electromagnetic field in accordance with ELV and ALs from the Directive 2013/35/EU (http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013L0035).

Proposal 2: Propose to the Ministry of Work and Social Policy and the Ministry of Health to adopt a new rule book about MRI safety. Similar rule book is developed in Macedonia for ionizing radiation safety, and it has been adopted by all ionizing radiation sites.

In this new by-law document special emphases should be put on few main points important for MRI safety:

1. To define exposure levels for typical MR devices (with special article for MRI exposure)
2. To define exposure levels for three modes of MRI operation (normal, controlled and research/experimental mode) for three categories of potentially exposed subjects:

- Patients for diagnosis/volunteers engaged in clinical trials and cares,
- Staff/employed workers and
- General public (visitors and educational visitors/students).

3. To define the MRI zones and labeling – MRI Facility Safety Design Guidelines (http://onlinelibrary.wiley.com/doi/10.1002/jmri.24011/pdf)

4. To categorize the occupationally exposed workers (level 1 and level 2) in accordance with their responsibilities and exposure during the procedure for MRI scaning.

The MRI exposure limits for patients, operators and volunteers are available from the Canadian safety Code 26 (http://www.hc-sc.gc.ca/ewh-semt/pubs/radiation/87ehd-dhm127/index-eng.php as well as in the White Paper on MRI Safety of the American College of Radiology (http://www.bic.mni.mcgill.ca/~mferre/fmri.html/acr_white_paper.pdf).

Proposal 3: To propose obligatory establishment of a Joint National MRI Safety Committee by the Ministry of Labor and Ministry of Health. Macedonia is a small country so it makes sense to have a centralized committee. Similar bodies exist at McGill University (https://www.mcgill.ca/neuro/research/research-services/magnetic-resonance-research-committee), Concordia University (http://www.concordia.ca/campus-life/safety/lab-safety/magnetic-safety.html), Medical College of Wisconsin (http://www.mcw.edu/MRI-Safety-Committee/About-MRI-Safety-Committee.htm) and many other.

Proposal 4: To propose the obligatory appointment of MRI Safety ɜ Officers (MRSO) in all hospitals/facilities where MRI procedures are performed, independently of their purpose (clinical diagnosis or research activities). The role and responsibilities of MRSO would be complementary to the activities of the Radiation Safety Officers, because in context of the Macedonian clinical practice, MRI and X-Ray facilities are part of a single unit for diagnostic imaging. The MRSO should work under the supervision of the occupational safety expert (OSE) in the hospital or outpatient health care organization. In accordance with the Macedonian Occupational safety and Health Act, OSE must be appointed (or subcontracted) by the director/head/manager of the organization.

1.2. Submission of Premarket Notification for Magnetic Resonance Diagnostic Devices

The magnetic resonance diagnostic devices (MRDD) which will be used for research purposes (in addition to clinical use) must fulfill all requirements included in a relevant premarket notification and appropriate standards for safety characteristics for Magnetic Resonance Diagnostic Device (MRDD). The principal components of the MRDDs include the main magnet, shim and gradient systems, RF transmitter and receiver, transmit and receive coils, power supplies, computer and software. The standards and detailed instruction for functioning of all MRDD's components should assist radiologists and MRI imaging specialists in performing optimal MRI examinations.Below are several examples for the Submission Of Premarket Notifications for Magnetic Resonance Diagnostic Devices published by Food and Drug Administration, Center for Devices and Radiological Health - U.S. Department Of Health and Human Services and Standard for Magnetic Resonance Imaging of the Canadian Association of Radiologists (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm073817.htmandhttp://www.car.ca/uploads/standards%20 guidelines/20110428_en_standard_magnetic_resonance.pdf)

Proposal 1: National responsible bodies/inspectors should be trained for checking all the manufacturer's requirements which are listed in a premarket notification before giving formal approval for start of the clinical/research use of the MRDD.

2. Standards and Standard Operating Procedure (SOP)

The term **Standard Operating Procedure**, or **SOP**, is used in a variety of different contexts, including healthcare. The International Conference on Harmonisation (ICH) defines SOPs as "detailed, written instructions to achieve uniformity of the performance of a specific function". SOPs get usually applied in pharmaceutical processing and for related clinical studies. The focus is always set on repeated application of unchanged processes and procedures and its documentation. In the case of research studies, research directors or principal investigators are mainly responsible for SOPs. They are sometimes called safe work methods statements (SWMS). They are usually preceded by various methods of analyzing tasks or jobs to be performed in a workplace, including an approach called "job safety analysis", in which hazards are identified and their control methods described. Standard operating procedures must be suitable and accessible for users (user friendly) and be easily accessible in a written form. MRI accreditation needs to have developed SOPs. All accredited health/MRI facilities, as a prerequisite of ISO 9001,develop their own SOPs based on the their own practices and work specificity. Good set of SOPs is available at Concordia University https://perform.concordia.ca/GettingStarted/pdf/compliance/PC-SOP-IM-003-V02%20MRI%20 SAFETY%20PROCEDURES%20AT%20PERFORM.pdf; Robarts Imaging - http://imaging.robarts.ca /3t/resources; Medical College of Wisconsin - http://www.mcw.edu/MRI-Safety-Committee/ Procedures.htm).

Proposal 1: Joint National MRI Safety Committee should develop Generic Set of SOPs as a model for MRI end users and assist them to develop their own SOPs. This should be a prerequisite for accreditation of MRI facilities/methods which will make them to be eligible and internationally recognized as MRI research units. This should be a prerequisite for establishment of the planned Regional MRI Research Center. The generic SOPs should have individual procedures for:

2.1. Qualification of personnel

According to the Canadian Association of Radiologists MRI Standard, the qualified MRI eam should be composed of:

- Radiologist
- MRI physicist
- MRI medical radiation technologist
- MRI field engineer

Resource:
(http://www.car.ca/uploads/standards%20guidelines/20110428_en_standard_magnetic_resonance.pdf).

In Macedonia, there are medical physicists working in all radiological units on a contract basis. Only few of the diagnostic imaging centers have their own medical physicists, mainly in private hospitals. Initial acceptance testing prior to any clinical scanning is not part of the regular procedure; there is no field engineer with responsibility for calibration, and preventive maintenance (PM) at regularly scheduled intervals. Therefore, the structure of the MRI team and their everyday duties must be described in SOP's for MRI staff and their responsibility

(http://www.mcw.edu/FileLibrary/ Groups/MRISafety/TextFiles/revisedsops/StudyPersonnelResponsibility11-14.pdf

2.2. Quality control system

The objective of an MR quality control (QC) program is to provide a series of tests and measurements on a regular basis aiming to determine if the MR system is performing in a reproducible and predictable manner. Quality control tests should be conducted under the supervision of the medical physicist (if present on site), with a review at least every six months by the supervising radiologist.

Acquisition of the test data can be done by a MRI technologist (all MRI technologists should be trained to run and assess basic QA/QC scans) who has been trained by the MRI physicist in the QA/QC acquisition procedure. Testing is best done on a routine schedule, first thing in the morning, prior to clinical scanning. This requires an ACR phantom and MRI physicist. A quality control program with written procedures and logs shall be maintained at the MR site.

Resources: American College of Radiology: The MRI Accreditation Program evaluates staff qualifications, quality control, MR safety policies and image quality

(http://www.acraccreditation.org/Modalities/MRI) and Inter societal Accreditation Commission MRI (http://intersocietal.org/mri/standards/IACMRIStandards2015.pdf).

2.2.1. Quality control test

The following quality control tests shall be performed and documented:

a. measurement of central frequency
b. measurement of system signal-to-noise ratio on a standard head or body coil
c. table positioning
d. geometric accuracy
e. high and low contrast resolution
f. artifact analysis

2.2.2. Performance evaluation test

The following quality control tests shall be reviewed by the medical physicist annually, and after any major upgrade or major change in equipment:

a. review of daily quality control testing records
b. measurement of image uniformity
c. measurement of spatial linearity
d. measurement of high contrast spatial resolution
e. measurement of slice thickness, locations and separations
f. assessment of image quality and image artifacts
g. eddy current compensation
h. system shim

In Macedonia quality control of the MRI equipment and services is performed on an irregular basis from the supplier of manufacturer's service. Below are some resources for appropriate

quality assessment tests, including the American Association of Medical Physicists: Quality Assurance Methods and Phantoms for Magnetic Resonance Imaging:
(https://www.aapm.org/pubs/reports/RPT_28.pdf)
(http://www.ncbi.nlm.nih.gov/pubmed/21767198;
https://www.aapm.org/pubs/reports/RPT_100.pdf)
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3047180/).

Last year the American College of Radiology published an MRI Quality Control Manual (2015) with detailed description of the role, responsibilities, type and periodicity of the quality control test of the radiologists, technologists, medical physicists and field engineers. It would be the corner stone for development of the Generic SOP for MRI quality control in MKD.
(http://www.acr.org/~/media/ACR%20No%20Index/Documents/QC%20Manual/2015_MR_QCManual_Book.pdf).

The SOPs for quality assessment would include the procedures for everyday maintenance of the MRI system (http://imaging.robarts.ca/3t/resources):

- System Start-up and Restart,
- System Shutdown/END OF DAY,
- Equipment Handling and Procedures,
- Gradient Insert Installation and Removal,
- Data Handling and Storage/Anonymization and Editing Subject Data (for research purpose only).

2.3. Basic MRI safety standards

The information about hazards, potential biological and health effects as well as a basic safety consideration related to the MRI zones, and categorization of the exposed workers were recently published by me in the official journal of the Macedonian Academy of Sciences and Arts.

(http://www.manu.edu.mk/prilozi/jully2012/MAGNETIC%20RESONANCE%20IMAGING%20SAFETY%20PRINCIPLES.pdf.

However, this paper does not have any law or by-law power and cannot impose the implementation of described safety issues. Therefore, the above considerations should be included in the SOP for MRI Safety Practice. A similar documenthasbeen published by the American College of Radiology in 2013, called the Guidance Document on MRI Safe Practices

(http://onlinelibrary.wiley.com/doi/10.1002/jmri.24011/pdf).

In accordance with the safety MRI procedure, three groups of SOPsare proposed:

- SOPs for safety issues due to medical devices incompatible with magnet
- SOPs for safety issues due to high static magnetic field strength
- SOPs for safety issues due to hardware

2.3.1. Safety issues due to medical devices incompatible with magnet/devices screening

There are medical devices, implants and objects that are incompatible with the MR environment. Anyone with any of these devices should indicate so before entering the facility, and may not proceed beyond the magnet room door unless the object can be safely removed or identified to be MR safe. The screening would be described in the appropriate SOP, including the list of magnet incompatible devices: aneurysm clip(s), Implanted cardioverter defibrillator

(ICD), electronic implant or device, magnetically activated implant or device, neurostimulation system, spinal cord stimulator, cochlear implant or implanted hearing aid, insulin or infusion pump, implanted drug infusion device, any metallic fragment or foreign body, any external or internal metallic object, etc. Screening form (for staff, patients and visitors) should be synchronized with this SOP for safety issues due to medical devices incompatible with magnet (see below)

2.3.2. Safety issues due to high static magnetic field strength/object screening

Appropriate SOP should be developed about the safety procedure in regard to the possible effect of static magnetic field on ferrous objects. The static magnetic field is always on, making it a permanent potential risk for staff, patients and volunteers. All metallic objects with ferrous components have the potential to become projectiles in the MR environment. There are several metals that are non-ferrous: titanium, copper, gold, silver, aluminum, brass and lead. It is mandatory to remove all personal metallic objects from the person (staff, patient or research volunteers) before crossing through the doorway into the magnet room. This includes the articles like: cell phone, keys, eyeglasses, jewelry, watch, credit and bank cards etc.).

In this standard procedure the use of metal detectors should be described. The usage of the conventional metal detector in the MR environment is not recommended. However, ferromagnetic detection systems capable of detecting very small ferromagnetic objects and differentiating between ferromagnetic and non-ferromagnetic materials would be useful, especially as an adjunct to thorough and conscientious screening of persons and devices approaching Zone IV (http://onlinelibrary.wiley.com/doi/10.1002/jmri.24011/pdf).

2.3.3. Safety issues due to hardware (electricity, fire…)

Dangerous and potentially lethal levels of electricity exist in a magnetic resonance system. It is therefore imperative that all individuals working in magnetic resonance facilities be aware of these dangers and become knowledgeable regarding safety issues concerning electricity. There is a risk of electrical shock from extremely high voltage, possibly causing severe injury or death to a person and damage to the magnetic resonance equipment.

Current carrying cables, connections and junction points in the vicinity of the main magnetic field are particularly susceptible to damage due to the extreme Lorentz forces created through the normal operation of the system. Periodically, the effects of the prolonged mechanical fatigue will result in breakage causing electrical arcing, sparking and high heat levels before the system can shut down.

Therefore, there is a potential for personal injury and thepossibility of a fire being ignited. The appropriate SOP for emergency fire should be developed. This SOP should have a special section on the use of fire protection equipment when the magnet is still on. The procedure for stopping the magnet in case of uncontrolled fire, should also be describe.

2.3.3.1. Emergency quench procedures

The SOP for emergency quench is essential for protecting the lives and properties in case of safety issues due to hardware or in case of environmental emergencies. In both casesit is necessary to have a proper procedure about who will decide to stop the magnet and how the

procedure needs to be performed. There are two possible situations when the magnet should be stopped and emergency button must be pressed, and two different SOP should be developed:

- emergency quench standard operating procedure if any individual is pinned to the magnet, trapped or in a potentially life threatening situation by a non-removable ferrous object. If the person is injured, the operator must apply first responder principles. If the victim is not responding, not breathing and has no pulse, the following procedure must be additionally outlined in this or separate SOP,
- emergency quench standard operating procedure if there is a fire in the magnet room that cannot be contained using the nonmagnetic fire extinguisher and requires the assistance of the fire department.

2.3.4. Screening form for MR personnel, patients and non-MR personnel

The best approach to minimize the possible consequences from safety issues due to medical devices incompatible with magnet/devices, high static magnetic field strength, hardware or quench, is to develop appropriate and detailed screening forms for staff, patients and visitors.

In Macedonia a screening procedure for patients is performed in all MRI facilities. There have been no registered incidents during the MRI clinical procedures. There is no standardized screening procedure for staff and visitors. The standardized screening form for personnel, patients and non-MR personnel should be developed and the procedure about the use of this form should be described (who performs the screening procedure, how and when) in the form of a generic SOP. This screening form should be developed and put in practice on mandatory bases for all MRI facilities in MKD. Based on the documents surveyed at the Montreal Neurological Institute and the Montreal Heart Institute, this SOP should contain minimum: identification of the screened person, data about the previous MRI scanning, data from the related medical history (injuries with metal object, past operation, allergies associated with contrast agents), pregnancy information, MRI hazards check (information about different kind of implants, pacemakers, body piercing, IUD, tattoos, colored contact lenses etc.). The information/questions for patients/volunteers should be part of this screening. Special reminders should be used abouteyeglasses, underwire bra, clothing with metallic zippers, belts, buttons etc. A sample screening form can be found in Appendix A of the Canadian Association of Radiologists Standards for Magnetic Resonance Imaging - http://www.car.ca/uploads/standards%20guidelines/20110428_en_standard_magnetic_resonance.pdf.

The screening process and screening forms for patients, non-MR personnel, and MR personnel should be essentially identical. But, specific circumstances related to the MRI scanning impose development of the appropriate SOPs. In this context, the SOPs for facility visitor approval should be developed, too. All these procedure (SOPs) should contain at least a title, version, revision chronology, scope and procedure for two categories of visitors:

- Those entering the control room only and not entering the magnet room.
- Those with intent of entering the magnet room.
  (http://www.imaging.robarts.ca/3t/sites/imaging.robarts.ca.3t/files/110.06%203T%20MRI%20SOP%20Visitor%20Approval%20Procedures%2006June2013.pdf)

The SOPs for MRI screening should be connected with the SOP for patient and staff safety. The ICNIRP Statement from 2004 and its amendment from 2009 give very detailed information about the safety of these categories of users (http://www.icnirp.org/cms/upload/publications/ICNIRPMR2009.pdf).

2.3.5. Emergency/incident procedures and procedures for other health/behavior related issues(medical emergencies) SOPs

Emergencies are situations in which one or more persons require medical attention, evacuation, or immediate interruption of work to prevent injury or damage to equipment (e.g., magnet quenching).

Emergencies which require medical attention may arise from magnetic fields, flying objects, cryogen spills, implanted medical device issues, magnet quenching or, in the case of patients' or research participants' change of behavior, responsiveness and health status. In MKD there are no standard procedure for any of these sitiations. Therefore, few SOPs should be developed, appropriate for each of those specific situation as follows:

- Cardiac arrest
  - immediately remove the patient from zone IV while initiating cardiopulmonary resuscitation
  - define safe area for resuscitation that is not in zone IV.
- Contrast agent safety/Gadolinium based contrast agents for MRI
  - Patients at increasing risk
  - Precautionary principles for patient at high risk
    - Severe Renal Disease, Gadolinium-Based MR Contrast Agents, and Nephrogenic Fibrosing Dermopathy/Nephrogenic Systemic Fibrosis (NFD/NSF)http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm456012.htm
  - Prior contrast agent administration consent form completed
  - Medical questionnaire completed and reviewed by physician
  - Physician present during the procedure
- Claustrophobia
  - Non-pharmaceutical management
  - Immediate access to 'panic' button
  - Sedation
- Sedation
  - Patient preparation
  - Standard regime and appropriate sedative agents and doses
  - Monitoring of the sedated patients by appropriately trained medical staff
- Analgesia and Anesthesia

Adult and pediatric patient anxiolysis, sedation, analgesia, and anesthesia for any reason should follow established ACR, American Society of Anesthesiologists (ASA), and TJC standards (http://www.asahq.org/quality-and-practice-management/standards-and-guidelines).

- Pregnancy issues
  - pregnancy of staff (should not remain in exam room during scanning, otherwise may work normally; may opt out of all scan room work in the first trimester
  - pregnancy of patients/volunteers (it may be appropriate to formally obtain informed consent from the patient in these circumstances; it is considered prudent to avoid MRI examination in the first trimester).

2.3.6. MR Facility Emergency Preparedness Guidelines/SOPs (environmental emergencies)

Healthcare facilities have a unique obligation to minimize the disruption from disasters and hasten their ability to restore critical patient care services when interrupted. Those charged

with the operation of MRI facilities have the added complexities of protecting not only the staff and structure, but also the equipment which may be extraordinarily sensitive to changes in its environment, including vibration, power supply, and water damage. Separate SOPs should be developed in case of:

- Water damage from roof-failure, burst pipes, floods, storm surge or rising river,
- Structural damage
- Power outage
- Quench
- MRI emergencies requiring fire and/or police response.

Macedonia has a history of flood emergencies and earthquakes, and particularattention should be paid to power outages because the hospitals don't have continuous electricity supply in all MRI facilities. (http://onlinelibrary.wiley.com/doi/10.1002/jmri.24011/pdf).

3. Procedure for Operator Training – Minimum requirements for MRI system operators

Magnetic Resonance Imaging (MRI) at high magnetic field strengths presents unique hazards to both research subjects and individuals working within and around the MRI system. Consequently, the potential for serious personal injury is present due to the sheer size and strength of the static magnetic field along with the flexibility of the research system and associated peripheral hardware.

Training is a key element of the MRI facility safety. In Macedonia there are no documents, papers, procedure or standards that require training of the MRI staff. Therefore, in the near future we should determine (as part of a rule book for MRI safety) the mandatory requirement for MRI training and retraining in regular two year intervals**. An** MRI safety training course will be held onsite on a regular basis with content determined by the facility staff (according to the proposed rule book for MRI safety). Records for the attendance of course and the results of the (re)exam would be kept in a personal staff' file. The proposed syllabus for the minimum training course is part III of this report.

II. MRI ethics standards

II.1. National Advisory Council on Human Research Ethics

As with any complex and evolving technology, the use of magnetic resonance imaging (MRI) for research raises important issues concerning the protection of human subjects or participants. In view of the increasing involvement of MRI technology in human subjects (HS) research, particularly in non-clinical settings, the need to consider safety and ethical issues related to both the administration of MR (magnetic resonance) facilities and the use of these facilities for research is very important.

In Macedonia, the Medical Faculty at the University St. Cyril and Methodius is responsible for the operation of the Ethics Review Committee for human research, and its main responsibility is to approve new protocols and clinical trials. The committee follows a by-law document where the procedure for approval of new protocols is described, followed by the standardized application form. This document provides specific provisions regarding the conduct of clinical trials, including multi-center trials on human subjects involving medicinal products as defined in Article 1 of European Directive 20/01/EEC (http://ec.europa.eu/health/files/eudralex/vol-

1/dir_2001_20/dir_ 2001_20_en.pdf) in particular relating to the implementation of good clinical practice. Unfortunately, this document does not apply to non-interventional trials like MRI research, and has a limited application to only one university setting (Medical Faculty in Skopje). There is no similar document for research ethics in other clinical settings and facilities. This document does not contain standard forms for individual informed consent, nor the essential information that must be obtained from the participants in the research study (patients or volunteers).

*Proposal 1:*To propose to the Ministry of Health and the Ministry of Education and Science to establish a National Advisory Council on Human Research Ethics with main responsibilities to develop National Policies and Practices for Research Ethics (NPPRE) and follow the implementation of the ethical and legal aspects of research involving human subjects. The scope of competencies of this National Council would be to develop and to improve ethical practices in the country. This document would serve as a basic document with ethical standards that would be met by all research centers.

The main reason for establishment of the National Advisory Council on Human Research Ethics is the fact that Macedonia is small country and there are no human resources and competent experts for establishment of the Research Ethics Committees in all universities/faculties, research units and health care organizations where MRI research could be performed.

The NPPRE should contain: mandate and legal basis of the National Advisory Council, ethics framework with core principles, scope of research ethics review and competencies of the institutional review board, the consent process, fairness and equity in research participation, privacy and confidentiality, conflict of interest, key concept and ethics in qualitative research, clinical trials, research with biological human material, human genetics research.

The National Advisory Council on Human Research Ethics would be responsible for publishing of the Macedonian Textbook on Research in Ethics, based on the European Directive for implementation of good clinical practice in the conduct of clinical trials on medicinal.

Resources:

European Textbook on Ethics in Research (https://ec.europa.eu/research/science-society/document_library/pdf_06/textbook-on-ethics-report_en.pdf);

International Ethical Guidelines for Biomedical Research Involving Human Subjects (http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm)

Canadian Three-Council Policy Statement: http://www.pre.ethics.gc.ca/pdf/eng/tcps2-2014/TCPS_2_FINAL_Web.pdf and

McGill University Policy on the Ethical Conduct of Research involving Human Participants. (https://www.mcgill.ca/files/secretariat/Ethical-Conduct-Research-Human-Policy.pdf)

II.2. National Magnetic Resonance Research Committee

The growing use of MRI in everyday clinical practices in Macedonia, and the expected increase of MRI scanning for research purposes, imposes the need to consider safety and ethical issues related to both: the administration of MR (magnetic resonance) facilities and the use of these facilities for research. Therefore, a National Magnetic Resonance Research Committee (NMRRC) should be established as a working body of the National Advisory Council on Human Research

Ethics or as an independent committee of the Ministry of Health and Ministry of Education and Science.

Proposal 1: To establish a Magnetic Resonance Research Committee

Proposal 2: To establish an Institutional Review Board (IRB) in all MRI facilities where a research study will be performed

Resources: NIMH – Bethesda: http://www.nimh.nih.gov/about/advisory-boards-and-groups/namhc/reports/mri-research-safety-ethics_33826.pdf

Main task of the Magnetic Resonance Research Committee will be to develop an MRI Safety and Ethics Manual, which will be used as a guideline for preparation of the study protocol. The second task of this Committee would be to review all research proposals for scientific validity, safety, and relevance to the scientific mission, after the approval from the Institutional Review Board.

The main task of this IRB should be to perform suitable evaluation of the scientific merit of the study protocol and to provide a Statement concerning institutional support to researchers in maintaining promises of confidentiality and to approve the initial review for submission of the research protocol.

Resources:https://www.mcgill.ca/medresearch/files/medresearch/institutional_support_to_researchers_in_maintaining_promises_of_confidentiality.pdf

II.3. Preparation of the Protocol for Submission to the MRRC

The study protocol is the blueprint that all researchers will follow. A study protocol is a document that describes, in detail, the plan for conducting the clinical study. The study protocol explains the purpose and function of the study as well as how to carry it out. Some specific things included in the protocol are the reason for the study, the number of participants, eligibility and exclusion criteria, details of the intervention or therapy the participants will receive (such as frequency and dosages), what data will be gathered, what demographic information about the participants will be gathered, steps for clinical caregivers to carry out, and the study endpoints. A single standard protocol must be used without deviation to ensure that the resulting data will be significant and reliable.

The following elements should be included in the study protocol:

I. Study purpose and rationale;
II. Description of study population, inclusion and exclusion criteria;
III. Sample size and how it was determined;
IV. Design and description of methodology;
V. Definition of end-points;
VI. Measurements and study instruments (questionnaires, data collection forms, etc);
VII. Data analysis plan;
VIII. Recruitment procedures including copies of advertisements;
IX. Details on confidentiality (ex. Is there a link to data and participant, where will data be maintained, who has access, for how long will the information be kept, etc.)
X. Statement on ethical considerations (ex. Study will be conducted according to ethical principles stated in the Declaration of Helsinki (2013), ethics approval will be obtained

before initiating study, consent forms will take into consideration the well-being, free-will and respect of the participants, including respect of privacy, etc); and

XI. References.

The study protocol is included in the Application for initial review for submission to the Institutional Review Board (IRB). A sample application form is available at: https://www.mcgill.ca/neuro/files/neuro/newprot.pdf

Each submission for initial support must also come with a:
Consent form -
https://www.mcgill.ca/neuro/files/neuro/mrresearch.engconsentrevisedmay08.pdf
Declaration of consent - https://www.mcgill.ca/neuro/files/neuro/en_consent_rev_dec04.pdf
MRI Questionnaire - https://www.mcgill.ca/neuro/files/neuro/en_ques.pdf

After the approval from IRB the research proposal should be reviewed by the National Magnetic Resonance Research Committee. The relevant document for submission of the research protocol are available at the Montreal Neurological Institute Research website. Relevant document are:

- McGill University Policy on Research Ethics - https://www.mcgill.ca/neuro/files/neuro/mcgillethic.pdf
- Procedures and Policies of the MNI/H Research Ethics Boardhttps://www.mcgill.ca/neuro/files/neuro/procpol.pdf
- Guidelines for Consent Document Preparationhttps://www.mcgill.ca/neuro/files/neuro/consentformprep.pdf
- MUHC Guidelines on Free and Informed Consenthttps://www.mcgill.ca/neuro/files/neuro/consent1.pdf
- Gradations of Adverse Events and How to Report them to the REBhttps://www.mcgill.ca/neuro/files/neuro/advevent1998-05.pdf
- Protocol Termination Report Form https://www.mcgill.ca/neuro/files/neuro/termrept.pdf
- Study Status Report: https://www.mcgill.ca/neuro/files/neuro/study_status_report.pdf

Other supplementary documents for research protocol review are available at: https://www.mcgill.ca/neuro/research/research-services/reb

III. MRI Occupational Safety Training Course Syllabus

It is important that all those entering the facility be aware of the presence of the field, as it cannot be detected in any way, i.e. magnetic fields cannot be felt, seen or smelled. Ferromagnetic objects brought into the magnet room could quickly become dangerous projectiles, and the magnetic field can also interfere with the operation of certain medical implants. Because of this, training is a key element of the MRI facility safety.

Due to the responsibility associated with operating the scanner, and the importance of the safety of the volunteer/patient and experimental support personnel, all operators are required to obtain and hold a valid Emergency First Aid Training Certificate and CPR Level A Training certificate. Operators are also required to complete Automated External Defibrillator (AED) training.

It is mandatory that all operators participate in and complete the MRI facility safety training course. The course will be held onsite on an annual basis with content determined by the facility staff. It is strongly recommended that trainees complete a basic MR or Medical Imaging course covering MR imaging physics and safety, ideally prior to or coincident with this training program. All relevant documentation and information pertaining to operator status will be kept with the MRI Facility Manager/Technologist in a secured file cabinet and held in strict confidence.

III.1. Level 1 Safety Training

To be eligible for Level 1 Safety Training, participants must be screened as safe to enter the MR environment by a Level 2 individual.

Level 1 Safety Training consists of the following:
a) Watch the first 12 minutes of the ISMRM MRI Safety Video (basic course)
b) Read the Standard Operating Procedures and sign indicating that you understand them.
c) Attend a Safety Instruction Session with the MRI Safety Officer. This session will include:
    - Overview of all Emergency Procedures and locations of Table Stop, Electrical Stop and Quench buttons.
    - Thorough review of how to make oneself safe to enter the magnet room.

After completion of Level 1 Safety Training the participant will:

- ✓ Know how to make him- or herself safe to enter the MR environment
- ✓ Understand the dangers of a static magnetic field
- ✓ Be familiar with the Standard Operating Procedures
- ✓ Know all emergency procedures including the operation of the table/sequencestop, electrical stop and quench buttons.
- ✓ Pass the Level 1 training test.

Restrictions of Level 1 Safety training include:

- The individual may not screen others to enter the MR environment.
- The individual may not operate the MR scanner on human or animal subjects; they may only operate the MR scanner on phantoms
- The individual must then be certified by either the Facility Director or the MRI Safety Officer
- Card access to Zone III will be granted after successful completion of Level 1 Safety Training

Level 1 Training Syllabus:
a) Emergency contacts and administration
b) Contact names and numbers
    - Location of the 3T MR suite
    - Calling 911 from lab phone or a cell
    - Reporting incidents
c) Basic MRI Device Components
    - Magnet, Table
    - Gradients
    - RF shield
    - Wave guides
    - Cabinets

- Console
- Coils

d) MRI Safety
   - Screening Self and equipment
   - Eye wash stations/shower
   - Location of fire extinguishers
   - Locations of emergency shutdown button

e) Emergency Procedures
   - Emergency procedure Fire CardiacArrest
   - Respiratory Arrest
   - Magnet Quench
   - System Problems, shutdown, water leaks etc., emergency shutdown buttons

f) Standard Operating procedure – introduction, scope of content, implementation in practice
g) Facility orientation (field work) – MRI zones, magnet room and coils, equipment room, supplies in a scan room, prep room, location of the gas cylinder…
h) Exam

III.2. Level 2 Safety Training

The prerequisite to Level 2 Safety Training is successful completion of Level 1 Safety Training.

Level 2 Safety Training consists of the following:
a) Complete the Level 1 Safety Training Test.
b) Watch the ISMRM MRI Safety Video (advanced course)
c) Shadow and receive supervision from a Certified Scanner Operator forapproximately 10 scanning sessions (adjusted based on past education andexperience).

This time must include the following tasks:
- Thorough review of how to screen others to be sure they are safe to gointo the magnet room.
- Assisting in MR system preparation.
- Supervised execution of scanning procedures
- Research participant registration
- Starting and Stopping measurements.
- Communicating with participant during scan session.
- Transfer of data to server.

After completion of Level 2 Safety Training the participant will:

✓ Know how to administer the safety screening form
✓ Know the dangers of rapidly changing (dynamic) magnetic fields.
✓ Be able to explain the MRI-specific language on the experimental consent formsand the non-research waiver
✓ Know how to look up medical implants to determine whether they are safe.
✓ Know how to screen subjects for foreign objects.
✓ Be familiar with procedures for incidental findings
✓ Pass the Level 2 training test.

Level 2 Training Syllabus

Due to the responsibility incurred when operating the scanner, and the importance of the safety of the volunteer/patient and experimental support personnel, all operators are required to

obtain and hold a valid Emergency First Aid Training Certificate and CPR Level A Training certificate. Operators are also required to complete Automated External Defibrillator (AED) Training. It is mandatory that all operators participate in and complete the MRI facility safety training course. The course will be held onsite on an annual basis with content determined by the facility staff. It is strongly recommended that trainees complete a basic MR or Medical Imaging course covering MR imaging physics and safety, ideally prior to or coincident with this training program. All relevant documentation and information pertaining to operator status will be kept with the MRI Facility Manager/Technologist in a secured file cabinet and held in strict confidence.

a) Level 1 completion

b) Basic Console Orientation

- Registration
- Browser
- Transferring data/Networking
- Burning DVD/CD's
- Service Desktop Manage
- Protocol Management
- Error Log
- Raw Data file Management

c) Coil/Phantom selection/setup

- Product versus Facility made coils
- Phantoms

d) Scanning a phantom from start to finish

- Coil and phantom selection
- How to register
- Protocol selection
- Selection of parameters
- Auto Prescan/Manual Prescan
- CV's/Control variables
- Image display, manipulation
- End exam, Transfer data, Delete data
- Return equipment and room to original status

Many other education/training materials, including two videos for level 1 and level 2 training, are available at the safety page of the International Society for Magnetic Resonance in Medicine (ISMRM). http://www.ismrm.org/resources/ismrm-smrt-mr-safety-resources-page/

Montreal, 01.03.2016

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