Unanticipated Problem Reporting

1. Introduction

1.1 The Centre for Functional and Metabolic Mapping (CFMM) Core at Western's Robarts Research Institute houses Canada's only collection of high-field (3T human) and ultra-high field (7T human; 9.4T and 15.2T animal) MR systems. The Centre is dedicated to establishing the anatomical, metabolic and functional characteristics of normal brain development and healthy aging across the lifespan; as well as establishing the brain basis of developmental, neuropsychiatric and neurodegenerative deficits. CFMM resources are available to grant funded scientific collaborations, as well as industry sponsored contract studies with appropriate Review Ethics Board (REB) or Animal Care Committee (ACC) approval.

1.2 As per UWO HSREB Guideline documentation, Unanticipated Problems are defined as any incident, experience, or outcome that meets all of the following criteria:

1.2.1 *Unexpected* (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents (e.g. - the REB approved research protocol and informed consent document[s], Investigator Brochure, Product Monograph, Device Manual, etc.); and the characteristics of the research participant population being studied and;

1.2.2 *Related or possibly related* to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the [investigational product(s)] or procedures involved in the research) and;

1.2.3 *Suggests* that the research places research participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

2. Protocol Deviations

2.1 *Protocol deviations* are changes to a study that have not undergone ethics review and clearance. These are normally unanticipated or unintentional changes.

2.2 *Minor protocol deviations* generally impact administrative and logistical aspects of the study such as a study participant missing an appointment or changes in appointment dates.

2.3 *Major protocol deviations* may impact the research protocol, informed consent documentation or other study materials, which usually cannot be anticipated ahead of time and are often necessary to ensure the safety and welfare of the participants. Examples of major protocol deviations include:

2.3.1 Changes in procedures required to eliminate immediate risk to participants
2.3.2 Enrolment of participants outside the protocol inclusion/exclusion criteria
2.3.3 Significant deviation in the informed consent process such as use of incorrect version of the letter or form.

2.4 Protocol deviations may occur as a result of intervention by the CFMM staff prior to or during the research participants MRI visit. It is the ethical responsibility of the CFMM personnel to report and follow up on any protocol deviation(s).

2.5 If a deviation of the study protocol occurs during the process of scheduling or performing an MRI scan, the CFMM Director or Level 2 MRI Personnel must notify the Principal Investigator of the finding by completing and forwarding Appendix 5: "Unanticipated Problem Reporting" Form.

2.6 Further information regarding Protocol Deviations can be found at:

Guidance_Document_Protocol_Deviation_Violation_2019Aug8.pdf

3. Adverse Events

3.1 Any undesirable experience or response by a study participant is considered an *adverse event*. These may be emotional, psychological, physiological or physical in nature and may include injury or a detrimental incident experienced by a research participant. These events are usually related to study participation or a result of the research procedures taking place.

3.2 In the event of personal harm to the research participant, as a direct result of taking part in the research study, all necessary medical treatment will be made available and accommodated by CFMM personnel (ie. apply first responder principles and/or escort to UH Emergency).

3.3 If an adverse event occurs during a research participant's visit to the CFMM, the CFMM Director or Level 2 MRI Personnel must notify the Principal Investigator of the event by completing and forwarding Appendix 5: "Unanticipated Problem Reporting" Form.

3.4 Further information regarding Adverse Events can be found at:

Unanticipated_Problem_Reporting_Adverse_Event_Guidance_v10July2018.pdf

4. Incidental Findings

CFMM Responsibilities

4.1 *Incidental findings* are defined as previously undiagnosed medical conditions that are discovered unintentionally and are unrelated to the current medical condition or reason for which the individual is being treated or undergoing imaging. Research MRI scans are a leading source of incidental findings. A recent study reported that 2.2% of research MRI brain scans yielded an incidental finding.[1]

[1] *Orme NM, Fletcher JG, Siddiki HA, et al. Incidental Findings in Imaging Research: Evaluating Incidence, Benefit, and Burden. Arch Intern Med. 2010;170(17):1525-1532.*

4.2 The CFMM staff are not trained or qualified to detect or diagnose pathologies, and a

radiologist does not routinely review the acquired images. Research MRI protocols generally do not include a full suite of clinical acquisitions, further limiting our ability to detect abnormalities. Our detection ability is therefore limited to the research protocol and to the training and experience of the Level 2 MRI Personnel.

4.3 An incidental finding may be detected either at the time the scan is collected or by research personnel at a later time. It is the ethical responsibility of both the Level 2 MRI Personnel and the researcher to report and follow up on any abnormalities detected.

4.4 If the Level 2 MRI Personnel notes an abnormality during the scan session, care should be taken to avoid alarming the volunteer or patient. The acquisition of additional scans should be avoided, unless the Level 2 MRI Personnel deems it appropriate and necessary to confirm or rule out the presence of an abnormality.

4.5 Upon completion of the scan session, the Level 2 MRI Personnel should report their findings to the CFMM Director or a Senior MRI Technologist, who will then review the images in an attempt to confirm the presence or absence of an abnormality. If an incidental finding is confirmed, the CFMM Director or Level 2 MRI Personnel will then notify the Principal Investigator of the finding by forwarding completed copies of both Appendix 4: "Incidental Findings Review" Form, and Appendix 5: "Unanticipated Problem Reporting" Form.

4.6 Clinical radiology reports of research scans conducted in the MRI Facility will NOT be issued unless they are requested via the procedure listed in Section 4.11.2 below. Appendix 5: "Unanticipated Problem Reporting" form will be completed by a Level 2 MRI Personnel and will be kept in a locked file within the facility.

4.7 Follow up MRI scanning will **NOT** be performed at the CFMM as a method to circumvent appropriate clinical care.

Principal Investigator (PI) Responsibilities

4.8 If the Level 2 MRI Personnel detects an incidental finding, the Principal Investigator (PI) of the study will be notified. Alternatively, the PI's research staff may identify an incidental finding at a later time and notify the PI of their finding.

4.9 If an investigator or their research staff detect an abnormality in a research subject's MR images but are unsure whether it is significant, they may request the CFMM Director or a Senior MRI Technologist to review the images and assist them in determining whether or not the subject should be notified of an incidental finding.

4.10 Once the PI has been made aware of an incidental finding, it is their responsibility to follow-up with the patient/volunteer and notify them of the finding.

4.10.1 Care should be taken to avoid unnecessarily alarming the individual, and terminology should be kept general and non-descriptive (i.e. "incidental finding" or "possible abnormality" rather than "brain tumor", "lesion", or "region of hyperintensity"). Keep in mind that we are not qualified to diagnose pathologies and cannot determine the significance of any abnormality detected.

4.11 The PI should contact the patient/volunteer directly to inform them that an incidental finding has been identified and advise them of their options for follow-up, which include the following:

4.11.1 If the Principal Investigator IS an **LHSC clinician**:

4.11.1.1 With the patient/volunteer's permission, the PI may supply the anatomical images directly to LHSC radiology along with a request for a "review of guest exam" through the internal system.

4.11.1.2 A radiologist will review the images, and a report will be sent directly to the subject's family physician. The report will detail the findings and whether any additional imaging or investigation is necessary, as well as the urgency of it, which the subject can follow up on with their family physician.

4.11.2 If the Principal Investigator is NOT an **LHSC Physician**:

4.11.2.1 The PI should recommend that the subject contact their family physician to notify them that an incidental finding was detected on a research MRI scan.

4.11.2.2 The PI may provide them with a copy of their anatomical images on a CD/DVD to give to their physician, as well as a copy of CFMM's Appendix 4: "Incidental Finding Review" Form.

4.11.2.3 Family physicians and non-LHSC physicians can submit the images to LHSC radiology along with a request for a "review of guest exam".

4.11.2.4 A radiologist will review the images, and a report will be sent directly to the subject's family physician. The report will detail the findings and whether any additional imaging or investigation is necessary, as well as the urgency of it, which the subject can follow up on with their family physician.

4.12 If the patient/volunteer does not have a family physician, the subject may be provided with a copy of their anatomical images on CD/DVD, as well as a copy of CFMM's Appendix 4: "Incidental Finding Review" Form, which can be taken to any walk-in clinic or to Staff or Student Health Services on campus. The subject should inform the physician that they participated in a research MRI scan and were informed of a potential incidental finding that requires follow up. The physician can then forward the images to LHSC radiology with a request for a "review of guest exam" (included in Appendix 4), and the report detailing the findings will be returned to the clinic.

4.13 Note that many family physicians are unsure how to submit the "review of guest exam" request and may instead opt to order a clinical MRI scan. This decision is at the discretion of the physician; however, providing your patient/volunteer with a copy of their anatomical images on a CD/DVD as well as a printout with the instructions in Section 4.11.2 above may assist them in this process and help avoid unnecessary clinical MRI scans from being ordered.

4.14 Investigators should avoid publishing images obtained from subjects identified as having incidental findings.

4.15 Principal investigators and the CFMM are not responsible for incidental findings that are detected, pathologies that may be present but are not detected, the effect or outcome of an incidental finding on the patient/volunteer, or for any costs that may be incurred by the patient/volunteer during the follow up or treatment of an incidental finding. By participating in a research MRI study, individuals are agreeing to the possibility of an incidental finding being discovered. If a participant does not agree to the potential risk of discovering an incidental finding they should not participate in the study.

Revision Chronology		
Version Number	Date	Changes
230.01	01 March 2010	First Version
150.02	07 April 2020	New Template
150.03	12 May 2020	Added Protocol Deviations, Adverse Events (TS, JG)
150.04	11 Feb 2025	Added 15.2T; Updated Appendix Numbers

CFMM Director Signature: 

Date: 11 – Feb – 2025