SRTP - Project Description Form #240

PART I:

Name of Schulich faculty member who will supervise the project	Jonathan Lau
Supervisor's Schulich, Western, Hospital or Lawson Email	jonathan.lau@uwo.ca
Schulich Department	Clinical Neurological Sciences

PART II - Project Description

Title of Project	Surgical outcomes after invasive investigation of epilepsy: clinical and image-based predictors

Background
Stereotactic neurosurgery is a subspeciality within neurosurgery that relies on accurately targeting structures within the brain. In 1965, Talairach and Bancaud described Stereoelectroencephalography (SEEG) surgery which involves implantation of diagnostic electrodes to determine the epileptogenic zone (EZ) in individuals living with drug-resistant epilepsy (Bancaud & Talairach, 1965; Cardinale et al., 2013). Lüders et al. (2006) defined the EZ as "the minimum amount of cortex that must be resected (inactivated or completely disconnected) to produce seizure freedom." (Lüders et al., 2006). To delineate the EZ, non-invasive techniques such as scalp EEG, MRI, neuropsychological data, and functional neuroimaging data are first used (Iwasaki et al., 2016). If there is a concordance between these measures that point to a specific cerebral structure, further invasive techniques are often not required, and neurosurgeons can perform a resection of the EZ. However, if there is a lack of concordance in the non-invasive measures, or if a better delineation of the EZ is required, invasive techniques may be considered.

Over the last decade, many North American epilepsy surgery centers have transitioned from subdural electrode implantations to SEEG. SEEG is less invasive than subdural electrodes and degree of invasiveness for implantation of grid/strip subdural electrodes and their inability to record the electrical activity of deep cortical structures (Hamer et al., 2002; Steven et al., 2007; Voorhies & Cohen-Gadol, 2013). Depth electrodes are less invasive, have a lower complication rate, and enable direct recording from cortical/subcortical structures (Cardinale et al., 2013).

The transition of North American epilepsy surgery centers from subdural electrode implantations to stereoelectroencephalography (SEEG) has been largely facilitated by technological advances including robots. Our center has recently demonstrated that the transition to robotic SEEG is safe and reduces operating room time.

Hypothesis
We hypothesize that favorable outcomes after SEEG, as determined by metrics of success from epilepsy surgery (Engel classification), are associated with the extent of resection or ablation relative to nearby neuroanatomical features as well as the density of sampling and treatment of the EZ.

Proposed Methodology
This study will use a validated open framework for morphological analysis of brain images and establish whether neuroanatomical features are associated with successful results from treatment after SEEG implantation. The proposed study involves a retrospective design. Retrospective anatomical T1-weighted (T1w) magnetic resonance images (MRI) of the brain will be available leveraging data from over 150 patients with epilepsy who have been investigated with SEEG, a subset of whom underwent subsequent surgery, including one-year clinical outcomes.

The study will use a validated imaging methodology developed by the Principal Investigator (PI) for accurately placing landmarks on standard anatomical MRI scans of the human brain known as the Anatomical Fiducial (AFIDs) protocol, which has recently also been validated in clinical MRI datasets with contrast-enhancement. The applicant will be responsible for performing AFID annotations of the retrospective datasets with supervision from the PI. He or she will assist with segmentation of the resection area in order to define the volume of the resection and relate the EZ with the AFID features of interest. We will focus on post-operative outcome (Engel classification) and common negative post-surgical consequences - such as verbal memory, naming ability and visual field defects - to evaluate prognostic success.

Expected Outcomes
We expect that the results of this clinical and image-based analysis will result in improved prognostic and predictive information about morphological parameters that will allow for more targeted treatment of patients with epilepsy. This work will result in novel contributions to the literature by providing quantitative metrics that have the potential to establish a specific relationship between extent of resection/ablation and outcome, measurable in millimeters. Overall, this project shows promise to inform decision making on the type of procedure to perform in patients with medically intractable epilepsy.

Research Environment – Description of the number of research personnel, primary location of research, size of lab, etc
The research will be performed at Robarts Research Institute in the lab of PI Dr. Lau, who is an early-career clinician-researcher. The student will be co-supervised by Dr. Ana Suller-Marti, who is a clinician-researcher and epileptologist with a focus on SEEG. The applicant will have access to resources in the lab including several graduate students and a postdoctoral fellow. The SRTP applicant will work closely with Dr. Lau and Suller-Marti that will leverage ongoing collaborations with imaging researchers (Drs. Khan and Peters) and their associated labs. Ethics approval has already been obtained as well as data anonymization of the relevant MRIs to the project. Opportunities to participate and observe prospective epilepsy surgery cases will also be available, which will help solidify understanding of the many considerations for optimal outcome in this patient group.

Names and titles of other individuals who will be involved with the research project?
Dr. Greydon Gilmore, Western University, Clinical Electrophysiologist

Can this project be done remotely?	Yes
Duration of Project	Two Summers

Expected Objectives/Accomplishments for Student for Year 1?
Learn AFID placement after training under the supervision of the PIs and lab members. learn how to segment areas of resection and interest in the brain, in this case related to the EZ for epilepsy. Annotation and quality control of semi-automated AFID placements for the external and internal datasets. Prepare an abstract for presentation at a national or international conference. Contribute as coauthor and collaborator on ongoing publications that use the AFIDs protocol for different purposes: surgical planning, validation of automated placements. Contribute to updating the clinical database for patients with epilepsy undergoing SEEG.

Expected Objectives/Accomplishments for Student for Year 2?
Become an expert in AFID placement after training under the supervision of the PIs and lab members. Become an expert at segmentation of areas of resection and interest in the brain, in this case related to the EZ for epilepsy. Contribute as coauthor and collaborator on ongoing publications as a coauthor that use the AFIDs protocol and resection area segmentation for different purposes. Opportunity for conference presentation and manuscript preparation.

PART III - Certifications

If the project will require any certification approvals from one or more of the following offices, please check the

appropriate box below.	- Human Ethics
Human Ethics: If you have the protocol information, please enter it below (or enter the status of the approval).	R-16-065 (107590) approved

Note: certification approval should be obtained prior to the start of the summer. Projects without this approval will not be a priority for funding.