SRTP Project Description
Summer 2016

Name of Supervisor: Ali Khan
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Project Title: Quantitative analysis of neuropathology and imaging in temporal lobe epilepsy

Project Description – include background, hypothesis, proposed methodology, and expected outcomes (one page maximum; you may attach a page to this form):

(see attached page 3)

Research Environment - Our lab is located in the Robarts Research Institute and we have 2 graduate students, 1 clinical resident, and 3 undergraduate thesis students working on various projects in neuroimaging. We also collaborate actively with neurologists, neurosurgeons, and neuropathologists at LHSC, and neuroscientists in the Brain and Mind Institute.

Expected Objectives/Accomplishments for Student for Year 1: Annotation of cortical lamina in histology of 20 temporal lobe epilepsy patients, quantification of neuronal architecture features using these annotations, clustering of these data to define digital histology signatures, and correlation of these signatures with clinical variables. This work will be submitted for presentation at the annual Organization for Human Brain Mapping meeting. Manuscript preparation will begin (literature review, introduction, part 1 of methods).

Expected Objectives/Accomplishments for Student for Year 2: The annotations from year 1 will be transferred to pre-operative and ex-vivo MRI images of the same patients, features from quantitative MRI will be extracted using these annotations, and classification methods will be applied to determine the ability of MRI to predict these digital histology signatures. Manuscript preparation (methods, discussion) and submission of this work to a high-impact neuroscience journal will be completed.

If REB approval is required for this project, please provide REB Number:
HSREB 6259
OR provide the status of the application for REB approval:

Note: REB approval should be obtained prior to the start of Summer 2016.

Please submit complete application form, together with an abbreviated CV (not more than 4 pages – please do not include your entire CV) to Stacey Bastien at srop-srtp@schulich.uwo.ca

**Background:** Surgical treatment of refractory temporal lobe epilepsy (TLE) presents many challenges in locating the epileptogenic focus and thus not all patients become seizure-free following surgery. It is believed that early seizure recurrence is due to inadequate identification or removal of the epileptic lesion(s) or network, which may suggest the presence of dual pathology (histological abnormalities in the neocortex of patients with hippocampal sclerosis) or error in localizing subtle neocortical lesions. Objective and quantitative microscopic characterization of the neocortex from TLE patients can help us understand the relationship between subtle dual pathologies and seizure-freedom, and can also help discover imaging signatures that can detect these pathologies in-vivo.

**Hypothesis:**

a) Quantitative characterization of cortical architecture in the neocortex of anterior temporal lobectomy patients will reveal distinct signatures in patients with poor surgical outcomes, and b) these signatures can be predicted with advanced quantitative imaging techniques.

**Proposed Methodology:** Our group has been investigating advanced imaging methods to probe the structure and function of the brain in temporal lobe epilepsy through our ongoing CIHR-funded study on quantitative imaging for epilepsy surgery. We have created sophisticated image analysis pipelines to allow correlation between histology from resected tissue and pre-operative imaging, and have also developed and published tools for quantifying cortical architecture using immunohistochemical staining.

In the first phase of the project, the student will make use of existing tools and data in our lab to annotate the laminar structure in neocortical histology slides from 20 TLE patients, and extract quantitative metrics based on neuronal density, size, clustering, and orientation. Data-driven clustering algorithms will be used to determine digital histology signatures, and relevant clinical parameters for patients with distinct signatures will be compared statistically (seizure freedom, hippocampal pathology, duration of epilepsy). In the second phase of the project (summer year 2), the student will investigate correlations of these signatures with in-vivo (3T and 7T MRI) and ex-vivo (9.4T MRI) quantitative imaging metrics, in order to assess which signatures can be predicted with MR imaging.

**Expected Outcomes:** This work will be submitted for presentation at the annual Organization for Human Brain Mapping meeting, and a manuscript prepared with the student as first author will be submitted to a high-impact neuroscience journal (e.g. see references below).

**Selected references from our group:***

Goubran M, ... Peters TM, Khan AR. *In vivo MRI signatures of hippocampal subfield pathology in intractable epilepsy.* Accepted for publication in Human Brain Mapping, 5 Dec 2015. Impact factor 5.969
