

a place of mind



# **Quarterly Report on Research Activities in the Adult Neurosurgery Program**

**January 1<sup>st</sup> – March 31<sup>st</sup> 2019**

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# 1. INTRODUCTION

This report contains up to date information on the ongoing research projects that are supported by the Clinical Research Coordinators (CRC) of the University of British Columbia's (UBC's) Division of Neurosurgery at the Clinical Academic Campus of Vancouver General Hospital (VGH) for the period of January 1<sup>st</sup> to March 31<sup>st</sup> 2019\*\*. The main objective of the report is to familiarize the staff of the Division of Neurosurgery of UBC with the current research activities that are being supported by their CRCs. The studies that are supported by the CRC in this report are divided into two categories of ongoing studies: prospective studies, and retrospective studies. The number of studies per category is presented in the table below.

<b>Number of Ongoing Studies</b>				
Prospective	Retrospective	Inactive or Complete Studies	Medical Student Projects	Total
12	11	5	4	32

Detailed description of the purpose, objective, budget and sample size of each study supported by the CRC is presented in the next four sections of this report.

\*\*This report does not encompass research projects in the Division's paediatric neurosurgery, functional neurosurgery and spine neurosurgery programs.

## 2. ONGOING PROSPECTIVE STUDIES

### 1. Timing of Mobilization After Burr Hole Drainage of cSDH:

PI: Dr. Akagami; Co-PI: Drs. Tu, Chang, Honey, Makarenko

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
N/A	N/A	Sep 14 - Sep 19	100	92	Yes	Active	N/A

This is a two treatment arm, randomized, prospective study to minimize re-do burr-hole drainage procedures and any other associated complications in patients with chronic subdural haematomas.

Primary Outcomes:

- Recurrence requiring re-do drainage within the 1<sup>st</sup> month post-operatively
- Recurrence requiring re-do drainage between the 1<sup>st</sup> and 3<sup>rd</sup> months post-operatively

The timing of when to mobilize patients after burr-hole drainage of chronic subdural haematomas remains controversial. Traditionally, patients have been subjected to delayed mobilization in order to allow for the theoretical re-expansion of the brain and to decrease recurrence. Timing of bed rest is not consistent among centres and varies from immediately after to 7 days after surgery.

The objective is to determine optimal timing of mobilization in CSDH patients following a burr-hole drainage.

*Enrolment has ended. A total of 92 participants were enrolled. Data analysis is underway.*

## 2. Adult Hydrocephalus Clinical Research Network (AHCRN):

PI: Dr. Zwimpfer; Co-PI: Dr. Toyota

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
N/A	N/A	Nov '14 -	perpetual	305	Yes	Active	N/A

A multi-centre and multinational registry that collects data on adult hydrocephalus patients to characterize the etiology, understand variability, progression, and current treatment practices for hydrocephalus patients.

The overall purpose of the Registry is to establish and maintain a hydrocephalus patient event database for the Clinical Centres of the AHCRN, a research network newly established to investigate clinical management of adult hydrocephalus.

### Primary Objectives:

- To describe the natural history and treatment response for adults with previously untreated congenital hydrocephalus
- To describe the assessment and treatment of patients with Normal Pressure Hydrocephalus (NPH)
- To describe the complications associated with shunt surgery
- To determine the role for treatment with Endoscopic Third Ventriculostomy (ETV)

The Registry will provide previously unavailable epidemiological information about hydrocephalus patients seen throughout the participating Clinical Centers. This information will provide the basis for multi-institutional studies to be carried out by the AHCRN that may ultimately improve the clinical care for adults with hydrocephalus throughout the world. The continuing collection of such information serves to provide data necessary for hypothesis generation and study design. Examples of preliminary study designs include, but are not limited to, the following: preliminary power analysis, sample size determination, and recruitment projections. Radiologic imaging data will provide a unique opportunity to assess aspects of adult hydrocephalus diagnosis, management, and outcomes.

### Accomplishments of Merit:

- VGH made UBC 1<sup>st</sup> site to have accomplish Neuropsychological Battery Administration Training
- VGH made UBC 1<sup>st</sup> site to complete Neuropsychological Battery Administration Quality Control

*There are 1259 participants enrolled in the AHCRN Registry at all participating sites.*

*Of those, 305 are from the VGH site with 29 patients enrolled in the last quarter.*

**3. TOCA 511 Study - A Phase 2/3 Randomized, Open-Label Study of Toca 511, a Retroviral Replicating Vector, Combined With Toca FC versus Standard of Care in Subjects Undergoing Planned Resection for Recurrent Glioblastoma or Anaplastic Astrocytoma:**

PI: Dr. Toyota; Co-PI: Dr. Yip

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	Tocagen (Industry)	Apr 16 - Dec 19	200 in Phase 3	0	Yes	Inactive	N/A

Name of Investigational Product: Toca 511, a retroviral replicating vector (RRV) expressing a yeast-derived, codon-optimized cytosine deaminase (CD) prodrug-activator gene, in combination with Toca FC (flucytosine) extended-release tablets.

Primary Objective: To compare the overall survival (OS) of subjects treated with Toca 511 combined with Toca FC to subjects treated according to standard of care after tumor resection for recurrence of glioblastoma or anaplastic astrocytoma.

Methodology: This is a multicenter, randomized, open-label study of Toca 511 and Toca FC versus standard of care (SOC) that comprises Investigator's choice of either single agent chemotherapy (lomustine or temozolomide) or bevacizumab administered to subjects undergoing resection for first or second recurrence (including this recurrence) of glioblastoma or anaplastic astrocytoma. Subjects will be randomized at the time of surgery in a 1:1 ratio to receive either Toca 511 and Toca FC or control. Repeat scans will be obtained every 6 weeks for the first year and every 3 months after that.

Subjects may receive any standard of care treatment following progression or discontinuation from study due to toxicity. Crossover to the Experimental arm is not allowed, unless the primary endpoint is met and the Sponsor notifies the sites.

*Enrolment has ended, no patients were enrolled at the VGH site.*

#### **4. Quality of Life in Patients Diagnosed with Unruptured Cerebral Aneurysms** **Prospective Single-Centre Series:**

PI: Dr. Gooderham; Co-PI: Drs. Dandurand, Redekop, Haw

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	TAAF (NGO)	Jan 16 - Dec 19	150	150	Yes	Active	N/A

Aneurysms may require endovascular or microsurgical treatment if ruptured, growing, symptomatic or of significant size. The goal of prophylactic treatment of an aneurysm is to increase the number of years with good quality of life.

The main goal of the present study is to identify how does the diagnosis of an unruptured cerebral aneurysm and its subsequent treatment impact quality of life as measured by SF-36 and EQ5D in patients. We aim to quantify if the impact in quality of life varies overtime. We aim to verify if the choice of technique (endovascular vs microsurgical) has an impact on quality of life in the short and long term. We will explore the relationship with other variables such as gender, medical comorbidities, aneurysm location, and postoperative complications.

Quality of life will be assessed via the SF-36 and the EQ5D tool at time 0 (time of diagnosis) and at 1 year for patients with an untreated cerebral aneurysm. Quality of life will be assessed via the SF-36 tool at time 0 (time of diagnosis), 6-8 weeks postoperative follow-up and at 1-year postoperative follow-up in the patients who have been treated. The latter group will be divided in 2 sub-groups: endovascular and microsurgical (clipping).

*There are 150 participants currently enrolled in the QOL Aneurysm Study, follow-ups are ongoing.*

**5. LAANTERN Registry:**  
 PI: Dr. Toyota; Co-PI: N/A

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	Monteris (Industry)	Jan 16 - Dec 19	150 (all sites)	15	Yes	Active	N/A

The NeuroBlate<sup>®</sup> System (NBS) is a minimally invasive robotic laser thermotherapy tool that is being manufactured by Monteris Medical. It employs a pulsed surgical laser to deliver targeted energy to abnormal brain tissue. To further understand performance and utilization of NBS in current standard of care, post-market multi-center registry called LAANTERN (Laser Ablation of Abnormal Neurological Tissue using Robotic Neuroblate system) is designed to collect baseline, procedural and follow-up data on patients that are already scheduled to be treated with NBS in observational manner for publication purposes.

This is a multi-center registry that will include data collection at baseline (prior to NeuroBlate<sup>®</sup> procedure, which is also referred as the index procedure), during index procedure, discharge and up to 24-month follow-up. Up to 1,000 patients may be enrolled at up to 50 study sites. Most of the Enrolment will occur prospectively; however, the data collection for patients who already underwent a procedure with NBS may also take place retrospectively. For example, if the patient already had a NBS procedure, he/she may be approached about study participation. If the patient agrees to participate in the study, the data collection will be initiated once Informed Consent Form (ICF) is signed (e.g., demographics, procedure, and discharge data will be collected retrospectively and future follow-up visits collected prospectively).

*There are 15 participants currently enrolled in the LAANTERN Registry.*



**6. Quality of Life in Patients Diagnosed with Moyamoya Disease: Cross-Sectional Study:**  
 PI: Dr. Gooderham; Co-PI: Drs. Dandurand, Yip

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	Rare Diseases Foundation	May 2017 – May 2019	100	23	Yes	Approved	N/A

**Purpose**

Moyamoya disease is a rare and chronic disease characterized by the progressive occlusion of intracranial vessels. The supraclinoid carotid arteries are the first arteries affected. It rarely affects the posterior circulation. Small collateral vessels begin to form at the base of the brain as the larger vessels become occluded giving it the characteristic appearance of a «puff of smoke» on angiographic radiological studies. This disease can present with ischemic stroke or intracranial hemorrhage depending on the age of the patient.

**Objectives**

The main goal of the present study is to identify how does the diagnosis of Moyamoya disease, its different clinical presentations and its subsequent treatment impact quality of life as measured by SF-36, EQ5D and 49-item Stroke-Specific Quality of Life Scale (SSQOL) in patients. We aim to verify if the choice of technique (direct or indirect bypass) has an impact on quality of life. We will explore other variables such as clinical presentation (incidental, ischemic or hemorrhagic), radiological features (cerebrovascular reserve and evidence of ischemic stroke), gender, medical comorbidities, postoperative complications and length of time after diagnosis and treatment.

*There are 23 participants currently enrolled in the study, 5 participants were enrolled during the last quarter.*

**7. Early Palliative Care Trial:**

PI: Dr. Brian Toyota; Co-PI: Drs. Rance, Ayling, See, Yeomans, Bunn, Sakaluk

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	May 2017 – May 2019	100	0	Yes	On Hold	N/A

**Purpose**

The purpose of this research proposal is to conduct a randomized trial of early palliative care for patients diagnosed with glioblastoma (GBM), which would be the first study of its kind in this patient population. The aim is first, to attempt to enhance the quality of life of patients with GBM. And second, to potentially increase survival after diagnosis with GBM.

**Design and Methodology**

The proposed study is a non-blinded randomized control trial where patients with newly diagnosed GBMs will be randomized to either early palliative care plus standard oncologic therapy or standard oncologic therapy alone. It is a collaborative effort between palliative care physicians, neuro-oncologists, and neurosurgeons. Patients with histopathology confirmed GBM will be recruited into this study.

*This study is currently on hold.*

**8. Evaluation of Quality of Life of Patients with Lesions Affecting the Optic Apparatus and Comparison with Unified Visual Outcome Scale (UVFS):**

PI: Dr. Ryojo Akagami; Co-PI: Drs. Gooderham, Makarenko

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	May 2017 – May 2019	60	27	Yes	Approved	N/A

**Purpose**

We have designed a Unified Visual Function Scale (UVFS) based on the definition of legal blindness and the fitness to drive as a quick, accurate, and easy-to-use tool for evaluating visual outcomes (Makarenko et al. 2017, in print). UVFS needs to be tested for inter- and intra-observer reliability, as well as its correlation to be able to reflect quality of life impact. Other scales such as Visual Function Questionnaire (VFQ-25) or Activities of Daily Vision Scale (ADVS) have been used in attempts to correlate visual function to quality of life, but these are also unsuitable for routine clinical use. This study hopes to correlate UVFS to these scales, as well as establish its reliability for capturing quality of life assessments.

**Objective**

We have two objectives. First, we will attempt to characterize visual outcomes of patients with lesions affecting the optic apparatus, and then investigate the accuracy of our new Unified Visual Function Scale to correlate with the visual quality of life data. We hope to demonstrate that the Unified Visual Function Scale is able to not only provide clinically useful information, but also reflect impact of vision on patient quality of life.

*There are 27 participants currently enrolled in this study – enrolment for this study has ended.*

## 9. **EVD Complications in Canada:**

PI: Dr. Ryojo Akagami; Co-PI: Dr. Makarenko

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	Jan 2018 –	500 (across Canada) 50 (VGH)	50	Yes	Approved	N/A

### **Context**

Placement of external ventricular drain (EVD) catheters is a common neurosurgical procedure typically performed in emergent situations for the treatment of hydrocephalus and raised intracranial pressure (ICP). The procedure is associated with a number of complications resulting in significant morbidity. Comprehensive, prospective studies are lacking in describing the incidence of these complications and associated risk factors. A multi-centre prospective study is required in order to adequately investigate the complication profile of EVD catheter placement.

### **Design**

This is a prospective multi-centre observational study to be conducted at 12 Canadian neurosurgical centres forming part of the Canadian Neurosurgery Research Collaborative (CNRC). The CNRC is a Canadian research network made up of 12 neurosurgery residents representing the participating sites, and supported by attending neurosurgeons. The CNRC is bound by an agreement signed by all residents to protect the confidentiality of data and privacy of patients.

### **Hypothesis**

This study hypothesizes that in patients with EVD-catheters placed urgently (e.g. in the setting of intracranial hemorrhage or traumatic brain injury), the rates of EVD catheter-related complications including EVD catheter infection, hemorrhage and misplacement are influenced by patient, catheter and operator-related factors as described above.

*There are 50 participants enrolled.*

## 10. Meningioma QOL Electronic Patient Reported Outcomes:

PI: Dr. Ryojo Akagami

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	Jan 2018 – ongoing	Perpetual	18	Yes	Approved	N/A

### **Purpose**

This is a prospective study to collect information on quality of life before and after treatment for patients with meningioma. Knowing the expected quality of life associated with this diagnosis in the short and long term will not only help physicians and patients make a decision regarding treatment, but also, prepare the patient for the upcoming hardship. The goal of our study is to identify ways we can improve patient quality of life while they are undergoing treatment (surgery, radiation, or observation under the care of a neurosurgeon) for meningioma.

### **Objectives**

The main goal of the study is to identify how does the diagnosis of meningioma and its subsequent treatment impact quality of life as measured by FACT-MNG in patients. We aim to establish a baseline for pre-operative quality of life in patients with meningioma and to determine the impact of surgical treatment and/or subsequent interventions on patient reported quality of life outcomes.

### **Hypothesis**

Our hypotheses are the following: 1) we hypothesize that patient quality of life will improve after surgery for resection of meningioma compared to the observational group; 2) we hypothesize that VisionTree will be a feasible, well-tolerate and efficient tool for measuring objective and patient reported quality of life outcomes after meningioma treatment.

*There are 18 participants currently enrolled in this study, 3 of them were enrolled during the last quarter.*

11. **Next Generation Sequencing for Rare Variants in Familial Intracranial Aneurysms:**  
 PI: Dr. William Gibson (UBC Medical Genetics; BCCHR), Co-I's: Drs. Redekop, Haw, Gooderham, Dandurand

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
Yes	HSFC	Aug 1 – ongoing	Perpetual	103	Yes	Approved	N/A

### **Purpose**

Several genes that predispose to aneurysms of the large blood vessels like the aorta are already known, and there are some rare genetic syndromes that predispose to brain aneurysms when other medical features (such as kidney cysts) are also present. However, there are no genes yet known that cause non-syndromic brain aneurysms. Our goal is to identify the first human gene(s) for isolated intracranial berry aneurysms.

### **Objectives**

Our two specific aims are to catalogue the spectrum of rare coding variants in families diagnosed with intracranial aneurysms, and to validate functional effects of the most promising variant(s) on cerebral vasculature using animal models.

*There are 103 participants currently enrolled in this study. 5 were enrolled this quarter.*

## 12. Operative Cerebrovascular Exposure by Canadian Neurosurgery Residents:

PI: Dr. Toyota, Co-I's: Drs. Gooderham, Makarenko

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	None	March 2018 – August 2018	Residents and PDs from every neurosurgical centre in Canada		Yes	Approved	N/A

### **Purpose**

Given this rapid changing landscape of cerebrovascular neurosurgery, the training of a new generation of neurosurgeons has also evolved. The extent of these changes however has not been well documented, and the expectation of graduating neurosurgical programs across Canada and North America still reflect the management paradigm of past decades. With this survey we hope to characterize the resident experience and exposure with open cerebrovascular neurosurgery, predominantly the treatment of intracranial aneurysms. We hope by gaining this insight we can provide feedback as well as steer the development of training curriculum to account for the shift in cerebral aneurysm management.

### **Objectives**

We have two objectives. First, we will attempt to characterize the overall operative exposure of Canadian neurosurgery residents to treatment of cerebral aneurysms. Second, we will contrast the extent of the volume of open vascular and endovascular cases at each major Canadian neurosurgical centre by surveying program directors at the respective institutions.

### **Hypothesis**

We suspect that while it will vary across the country, with emerging emphasis on endovascular management of cerebrovascular conditions, the exposure of residents will be limited to open surgical cases.

*30 residents and 10 program directors have responded to the survey.*

### 3. ONGOING RETROSPECTIVE STUDIES

#### 1. **Biomarkers in Malignant Brain Tumors Study:**

PI: Dr Toyota

Study period	Approvals UBC CREB/VCHRI	Charts reviewed /Sample Size	Status	Abstract/Paper/ Manuscript	Funding
Jun 15 Aug 18	Yes	151/151	Active	N/A	N/A

To conduct a retrospective clinical chart review of our institution's glioblastoma cases to compare the predictive and prognostic value of molecular markers to that of traditional histological diagnoses.

This is a retrospective chart review involving charts of patients with glioblastoma treated at VGH from 2010-2014. We have created a database to register basic patient demographics, treatment protocols and outcome. Specific to our study, we classified the tumors by classic histologic description and grading as well as new cutting edge diagnostic molecular and genetic analysis.

Based on this database, we will stratify the patients into outcome categories based on classical grading and newer molecular markers. A statistical analysis of this data will then be conducted in order to compare the predictive value of these classic histologic methods with the newer methods for patient outcomes. Quinn Parker was a summer student who had obtained UBC SSRP funding for the summer. The chart review has been completed, and we await statistical analysis.

#### 2. **Quality of Life after Surgery in Patients with Pituitary Tumors and Acromegaly:**

PI: Dr. Akagami; Co-PI: Dr. Fatehi

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Dec 15 Dec 18	Yes	63	Active	Published in the Journal of Neurological Surgery (2017)	N/A

Patients with pituitary tumors have been previously noted to report decreased quality of life (QoL). These studies have used a variety of validated questionnaires (such as SF36 and AcroQoL) to assess the physical, cognitive and psychological well-being of patients affected by functional and non-functional tumors. Predictably, QoL is variably affected by different types and extents of tumor. Studies which have focused on patients with acromegaly have generally shown improvement of QoL after treatment (GH<2ng/ml). However, it is not clear whether the improvement of QoL is primarily driven by the correction of hormonal imbalances.

This is a retrospective review of QoL after pituitary surgery in patients with acromegaly. Any patient that lacks the SF36 questionnaire will be contacted, consented and given a copy to complete. All charts of patients who have previously undergone this procedure with Dr. Akagami shall be assessed. Multivariate analysis will be used to determine the factors which most impact QoL improvement post-operatively. The chart reviews have been completed.



3. **Computational 3D Segmentation of Cerebral Vasculature for Evaluation of Cerebral Aneurysms:**

PI: Dr. Gooderham; Co-PI: Drs. Hamarneh, Chew, Mendelsohn

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jan 10 Dec 18	Yes	500	Active	N/A	None

The primary objective of this study is to develop computer software using advanced imaging analysis techniques that can accurately detect cerebral aneurysms on CTA scans. The secondary objective of this study is to develop computer software that can detect changes in the size and shape of aneurysms over time in the same patient.

We hypothesize that advanced imaging analysis techniques will be able to be applied to CTA scans to successfully and accurately detect cerebral aneurysms and compare their size and shape at different points in time in the same patient. The chart reviews have been completed.

4. **Trigeminal Schwannoma Study:**

PI: Dr Akagami; Co-PI: Dr. Makarenko

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Mar 16 Feb 17	Yes	30	Active	Published in the Journal of Neurological Surgery Part B: Skull Base (2017)	N/A

This is a retrospective review of trigeminal schwannomas that were operated on by Dr. R. Akagami with an open craniotomy approach between 2001-2015 at Vancouver General Hospital. Our aim is to characterize the clinical presentation against imaging findings, and document the natural history of the TS tumours with respect to management strategy that includes surgical resection, radiotherapy, and observation.

We have two objectives. First, we will attempt to characterize the patients' trigeminal schwannoma anatomy with respect to location in middle and posterior cranial fossae, and then investigate their outcomes following transcranial resection of tumour by Dr. R. Akagami. We hope to correlate the patient's clinical presentation with the tumour anatomy with respect to sensory and motor symptoms, and then compare these against those of the findings in literature. The chart reviews have been completed.

5. **Current Glioblastoma Outcomes in BC:**

PI: Dr. Toyota; Co-PI: Dr. Fatehi

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jul 16 – Dec 17	Yes	200	Active	Published	N/A

Glioblastoma remains a lethal diagnosis with well-recognized failures in truly effective curative strategies. However there have been incremental improvements over the past decade that has predicted 2.5-fold improvements in 2-year survival. This prediction was based on a handful of studies describing new treatment strategies and bio-marker revelations. Our study seeks to document the actual 'real-world' change in glioblastoma outcomes. The objective is to establish the overall and median survival of a current cohort of patients treated for glioblastoma in B.C. undergoing standard treatment algorithms. The chart reviews have been completed.

6. **Reliability of the Unified Visual Fields Scale (UVFS) Study:**

PI: Dr. Ryojo Akagami; Co-PI: Drs. Gooderham, Makarenko

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jun 2017- Jun 2019	No	30	Approved	In preparation	N/A

**Purpose**

This is a study in inter- and intra-observer reliability. We will select 30 de-identified patients with pituitary lesions affecting vision. We will obtain their last visual acuity and visual fields assessments (Goldmann's visual fields) following surgical resection, and a UVFS score will be assigned as a consensus decision by the study investigators. We will then perform additional individualized assessments done by two neurosurgeons, two neurosurgery residents, and two medical student trainees. The reviewers will be presented with a formal visual field assessment as well as visual acuity scores, and asked to assign the UVFS score. These will be presented 3 different times to limit recall bias (total of 90 scores will be applied).

**Analysis**

We will use three statistical tests to assess inter- and intraobserver reliability. The interclass correlation coefficient (ICC) will be used to measure both inter-and intra-observer agreement for total UVFS scores (two-way mixed effect model, in which people effects are random, and measures effects are fixed). Fleiss's kappa will be used for multiple raters to measure interobserver agreement, and Cohen's kappa will be used to evaluate intraobserver agreement.

7. **PICA Aneurysm Study:**  
 PI: Dr. Gary Redekop; Co-PI: Dr. Fatehi

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jan 2017 – Dec 2018	Yes	53	Approved	In preparation	N/A

### **Purpose**

Aneurysms found in the posterior inferior cerebellar artery (PICA) are a rare cause of subarachnoid hemorrhage. Treatment for this type of aneurysm may be microsurgical or endovascular. This decision is based on patient characteristics, aneurysm location and dimensions along with surgical/institutional experience. Knowing how patient outcomes are affected by the different treatments of PICA aneurysms would help physicians and patients in their decision regarding treatment options.

### **Objectives**

The main goal of this study is to determine whether there are outcome differences between surgically and endovascular treatment. We aim to determine whether patient characteristics or aneurysm features predict treatment choice and subsequently patient outcome through a single-center retrospective chart review of patients admitted to Vancouver General Hospital (VGH) with symptomatic PICA aneurysms. Due to advances in endovascular management in the past two decades, data collection was limited to patients admitted between 2005 and 2015. Variables collected include patient demographics, clinical presentation, treatment complications and length of stay. The chart review is ongoing.

8. **Basilar Tip Aneurysm Study: Case series, systematic review and meta-analysis:**  
 PI: Dr. Gooderham; Co-I: Dr. Dandurand

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jan 2018 – Jan 2019	Yes	150	Active	Manuscript in progress	N/A

### **Objectives**

This investigation aims at characterizing 1) radiological outcome stratified per treatment technique 2) clinical outcome per treatment technique 3) rate of retreatment per treatment technique 4) risk factors for retreatment 4) create a large pool of patients to characterize rare phenomenon such as progressive growth of basilar aneurysm despite adequate occlusion at first treatment.

### **Hypothesis**

Our hypothesis is the following: 1) radiological outcome will be better with the use of stent-assisted coiling vs coiling alone 2) Perioperative complications may be higher in the stent-assisted group, but the retreatment rate and rehemorrhage rate will be lower.

## Outcomes

We will assess the relationship between radiological and clinical outcomes with each endovascular and surgical technique. Relationship between covariates and outcomes such as, patient's demographics, clinical presentation, size and features of aneurysms, radiological characteristics, and postoperative complications.

### 9. Image Analysis and Machine Learning for the Evaluation of Brain Tumours:

PI: Dr. Toyota; Co-I: Dr. Fatehi

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jan 2018 – Jan 2020	Yes	300	Active	N/A	N/A

## Objective

The primary objective of this study is to develop computer software that can accurately compare images from various time-points. Specifically, this software will be used to assess changes in tumors over time. The secondary objective of this study is to develop a computer software that can stratify tumor type and patient prognosis based upon radiologic features. In order to develop the automated computer software, imaging analysis of 300 brain MRI scans will be necessary.

## Hypothesis

1. We hypothesize that advanced imaging analysis techniques may be applied to MRI and CT scans to accurately assess the size and growth of brain tumors at different points in time in the same patient.
2. Tumor characteristics on imaging will correspond with and ultimately help predict patient survival.

### 10. Surgical epilepsy: complications and long-term outcomes:

PI: Dr. Redekop; Co-I: Dr. Ayling.

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jun 2018 – Jun 2019	Yes	500	Approved	N/A	N/A

## Objectives

To document our rates of complications and results of seizure status in patients that have undergone surgery for epilepsy at Vancouver General Hospital since 2000.

## Hypothesis

Specific patient and surgical factors will be associated with peri-procedural complications as well as long-term seizure outcomes.

## Research Design

This will be a retrospective review of patients diagnosed with epilepsy and that have undergone a surgical procedure. Charts of patients who have been managed at VGH will be reviewed for demographic, treatment strategies, and imaging data.

### 11. Pituitary Adenoma Resection and Post-Operative Diabetes Insipidus:

PI: Dr. Gooderham; Co-I's: Dr. Akagami, Makarenko.

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Jun 2018 – Jun 2019	Pending	300	Not started	N/A	N/A

## Objectives

Our main objective is to characterize the rate of diabetes insipidus following endoscopic transsphenoidal resection of pituitary tumours and to analyze the amount of pituitary gland translation in the post-operative period. As our secondary objectives, we will assess clinical features and surgical outcomes among the cohort.

## Hypothesis

We hypothesize the rate of diabetes insipidus following transsphenoidal pituitary surgery can be correlated with the distance travelled by the pituitary gland and subsequently the pituitary stalk following resection.

## Research Design

This is a retrospective chart review of endoscopic transsphenoidal pituitary tumour resections by Drs. P. Gooderham and R. Akagami between January 1st 2010 and December 31st 2017 at Vancouver General Hospital. There is expected to be approximately 300 patient charts to be reviewed.

## 12. Decompressive Craniectomy for Malignant Brain Edema in the Era of Mechanical Thrombectomy

PI: Dr. Haw; Co-I's: Drs Redekop, Gooderham, Fields, Fatehi.

Study period	Approvals UBC CREB/VCHRI	Anticipated Enrolment	Status	Abstract/Paper/ Manuscript	Funding
Nov 2018- Nov 2020	Obtained	800	Active	N/A	N/A

### **Objectives**

The main goal of this study is to determine whether mechanical thrombectomy decreases the rate of malignant edema and the need for decompressive craniectomies. We propose a single-center retrospective chart review of patients admitted to Vancouver General Hospital (VGH) with ischemic stroke

### **Hypothesis**

It is hypothesized that the introduction of mechanical thrombectomy for ischemic strokes has significantly decreased the need for decompressive surgery. We also hypothesize that the greatest decrease is seen in patients with proximal middle cerebral artery occlusions.

### **Outcomes**

The primary outcome of this study is to determine whether patients who had mechanical thrombectomy had a lower rate of surgical decompression compared to those patients who received intravenous tPA and those who were observed without intervention. The long-term clinical outcomes of those patients who underwent decompressive craniectomy after an ischemic stroke will be assessed using the modified Rankin score (mRS).

## 4. INACTIVE OR COMPLETE STUDIES

### 1. The Digital Physiotherapist:

PI: Dr. Toyota; Co-PI: Drs. Zemmar, Eng

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	Mar 2017 – Oct 2018	400	0	CREB & VCHRI Pending	Hold	N/A

#### **Purpose**

The main goal of this project is to develop a database which will record everyday life movements of the upper extremity (arms and hands) and lower extremities (legs and feet). We will use this information to determine what “normal” movement is. We then compare impaired movement after CNS injury to the “normal” movement database to identify the weakness in the injured patient. That knowledge is then used to selectively train the injured brain circuits. We furthermore plan to develop a device which will allow the patient to do physiotherapy exercise using their cellphone and virtual reality glasses.

#### **Significance of Study**

Repetitive physiotherapy is key in order to gain neuroplasticity and repair impaired neuronal circuits that are damaged by CNS injury. Long waiting times for physiotherapists or inability to afford a private physiotherapy are known obstacles for patients. By developing a device that selectively identifies impaired muscle groups and allows the patient to carry out targeted physiotherapy from anywhere at any time, we aim to allow the patient to carry out repetitive physiotherapy and enhance neuroplasticity to improve functioning of those nerve cells in the brain that orchestrate the weakened motion. With this approach we hope to create a new and effective avenue to treat patients with CNS injury more effectively.

*This study has been put on hold.*

2. **Resident Activity Tracker Evaluation (RATE) Study:**

PI: Dr. Toyota; Co-PI: Drs. Mendelsohn, Redekop, Singhal, Gooderham

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	RDBC (NGO) BCSPQC (NGO) MD Financial (NGO)	Sep 15 - Aug 17	60	59	Yes	Completed	In submission

Medical resident work hour restrictions remains a large topic of debate in the Accreditation Council for Graduate Medical Education; and more importantly, also in the Royal College of Physicians and Surgeons of Canada.

An adequate number of hours of sleep play an important role in medical residents' performance, and quality of life. Formal changes to resident work-hours regulation have not been imposed for Canadian medical residents. On-call duties vary substantially across medical specialties further complicating the issue. The actual physical demands of resident on-call duties and the impact on sleep duration and number of interruptions have not been comprehensively investigated to date.

This study will be the first in literature to measure average and maximum heart rate, sleep duration and interruptions, and number of steps taken per day in medical resident trainees, across non-surgical and surgical specialties and when the residents are on or off call. Such novel results will help advance and guide current discussion on resident work hour restriction towards a more comprehensive conclusion.

*There are 59 residents currently enrolled in the RATE Study. The enrolment has been completed. The manuscript has been submitted.*



### 3. **CanTBI Biobank & Registry:**

PI: Dr. Toyota; Co-PI: Drs. Honer, Brubacher, Carrion, Wellington, Torres, MacKay, Walley; Coordinator: Angela Aquino

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
Yes	Brain Canada (NGO)	Jul 15 - ongoing	350	95	Yes	Hold	N/A

#### **Aim**

- 1) To develop a national biobank by linking existing regional biobanks.
- 2) The creation of a national database of patients with TBI.
- 3) To link the national biobank and database with health care utilization data.
- 4) To promote collaboration among TBI scientists

#### **Methods**

We will prospectively enrol infants, children and adults with mild, moderate and severe TBI from intensive care units, emergency departments and sports concussion clinics. Serum, cerebrospinal fluid, brain samples and DNA will be collected using standard operating procedures. We will expand current biobanks and develop new regional biobanks dedicated to TBI patients. A core data set will be collected electronically, linked to tracked biosamples.

### 4. **PET/CT & Neurosurgical Resection:**

PI: Dr. Toyota; Co-PI: Drs. Yip, Mendelsohn, Wilson, Bénard

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
Yes	Neuro-Onc. Fund (NGO)	Oct 2016 – Oct 2018	40	0	No	Hold	N/A

#### **Purpose**

To study the use of Positron Emission Tomography to improve the extent of resection for gliomas. The 11C-Methionine PET/CT tracer is an amino acid analogue that can visualize tumour not clearly identified on diagnostic MRI. Use of 11C-Methionine PET/CT will permit better surgical resection and lead to better survival for patients with gliomas.

#### **Primary Objective**

To assess the extent of surgical resection of gliomas with preoperative and postoperative PET/CT imaging with 11C-Methionine and 18F-Fluorodeoxyglucose (18F-FDG)

*This study has been put on hold.*

**5. Nicotine Replacement Therapy Clinician Survey:**

PI: Dr. Gooderham; Co-PI: Drs. Chang, Dandurand

Study period	Approvals UBC CREB/VCHRI	Charts reviewed /sample size	Status	Abstract/Paper/ Manuscript	Funding
Jul 16 Dec 17	Yes	50/50	Completed	N/A	N/A

Between 50-66% of aneurysmal subarachnoid hemorrhage (aSAH) patients are active smokers, a notable statistic considering that smoking tobacco more than doubles the risk of aneurysmal SAH. Smoking gives aSAH patients an increased risk of in-hospital complications such as vasospasm or delayed cerebral ischemia (DCI) as well as increased mortality if they continue to smoke after discharge. Therefore the use of smoking cessation therapies during their hospital stay is a critical aspect for their clinical outcome. At the moment our findings demonstrate however, that there is an insufficiency of any guidelines that exist on the management of tobacco dependence in patients hospitalized for aneurysmal SAH. We performed a systematic review of randomized and controlled observational studies evaluating the impact of nicotine replacement therapy (NRT) on clinical outcomes in patients hospitalized with aSAH which showed NRT generally improved or did not impact short-term outcomes in smokers with aneurysmal SAH.

The purpose of this study is to evaluate vascular neurosurgeons' practice and beliefs regarding nicotine replacement therapy in subarachnoid hemorrhage patients. We will be asking Canadian neurosurgeons with a practice encompassing the management of aSAH to complete an online questionnaire, which should take under 5 minutes to complete and is only 4 questions long. They will be approached via email with an attached consent cover letter, outlining the study and requesting them to voluntarily complete the survey. Their responses for the 4 questions will be anonymous and have no identifying information. Response rates for each of the multiple choice segments of the questions will be reported using percentages and qualitative descriptions of optional open-field textboxes responses will be displayed.

## **5. MEDICAL STUDENT PROJECTS**

### **1. Predicting Shrinkage in Vestibular Schwannomas**

PI: Dr. Ryojo Akagami  
Student: Vincent Ye, PGY-1 (Toronto)  
Funding: SSRP 2017

### **2. Low grade gliomas, natural history and response to treatment**

PI: Dr. Brian Toyota  
Student: Bohan Hans Yang, Y3 MS  
Funding: SSRP 2017

### **3. Pituitary Adenoma Resection – Is There Correlation between Post-Operative Pituitary Gland Descent and Diabetes Insipidus?**

PI: Dr. Peter Gooderham  
Student: Armaan Malhotra, Y4 MS

### **4. Surgical epilepsy: complications and long-term outcomes**

PI: Dr. Gary Redekop  
Students: Annette Ye, Y2 MS; Heidi Britton, Y3 MS

### **5. Rare Presentations of Ischemic Pituitary Apoplexy: A Case Series**

PI: Dr. Ryojo Akagami  
Students: Shamon Ahmed, Y2