Quarterly Report on Research Activities in the Adult Neurosurgery Program

April 1st – June 30th 2023

Prepared by

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June 30, 2023

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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 April 1st to June 30th, 2023**. 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.

Number of Ongoing Studies			
Prospective	Retrospective	Inactive or Complete Studies	Total
15	3	1	19

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 pediatric neurosurgery, functional neurosurgery and spine neurosurgery programs.

2. ONGOING PROSPECTIVE STUDIES

1. **<u>Quality of Life in Patients Diagnosed with Moyamoya Disease: Cross-Sectional Study:</u>**

   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 - Oct 2025	100	63	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 63 participants currently enrolled in the study, 4 participant were enrolled during the last quarter.

2. **<u>Timing of Mobilization After Burr Hole Drainage of cSDH: a randomized study:</u>**

PI: Dr. Ryojo Akagami; Co-I: Drs. Sadr, Chang, Craig, Rizzuto, Rebchuk, Joshi, Hounjet

Funding	Source	Study period	Anticipated Enrolment	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
N/A	N/A	July 2022 - Jun 2023	50	12	Yes	Active	N/A

Purpose

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 1st month post-operatively
- Recurrence requiring re-do drainage between the 1st and 3rd 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.

Objective

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

There are 12 participants currently enrolled in the study, 1 participant was enrolled during the last quarter.

3. **<u>Adult Hydrocephalus Clinical Research Network (AHCRN):</u>**

PI: Dr. Thomas Zwimpfer

Funding	Source	Study period	Anticipated Enrolment	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
N/A	N/A	Nov 2014 -	Perpetual	594	Yes	Active	N/A

Purpose
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.

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.

There are 2,132 participants enrolled in the AHCRN Registry at all participating sites. Of those, 594 are from the VGH site with 18 patients enrolled in the last quarter.

4. **<u>Next Generation Sequencing for Rare Variants in Familial Intracranial Aneurysm:</u>**
   PI: Dr. William Gibson (UBC Medicial Genetics; BCCHR), Co-I's: Drs. Redekop, Haw, Gooderham

Funding	Source	Study period	Anticipated Enrolment	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
Yes	HSFC	Aug 2017 -	Perpetual	280	Yes	Active	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 280 participants currently enrolled in this study. 12 were enrolled this quarter.

5. **<u>Neuroscience of the Human Brain in Health and Disorder:</u>**
   PI: Dr. Mark Cembrowski (UBC Dept. Cellular and Physiological Sciences); Co-I's: Dr. Redekop, Fatehi, Hirsch-Reinshagen

Funding	Source	Study period	Anticipated Enrolment	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
Yes	Grant - Internal Funds	Nov 2020 -	120	22	Yes	Active	N/A

Purpose
(1) Understand organization and function of the healthy (i.e., pathologically unremarkable) human brain at molecular, cellular, and circuit levels; (2) use this understanding of the healthy brain to interpret dysregulation during epilepsy.

Objectives
(1) Characterize the molecular, cellular, and circuit properties of surgically resected discard human brain tissue in healthy cortex, (2) Compare this to analogous characterizations in brain tissue from epileptic foci to identify molecular, cellular, and circuit dysregulation in epilepsy.

Research design
Non-diagnostic discard brain tissue from Dr. Redekop and his staff, obtained via standard surgical resections from informed consenting participants, will be de-identified by Dr. Redekop or a member of VGH research staff, and via Dr. Hirsch- Reinshagen and VGH pathology,

received by Dr. Cembrowski to be used in neuroscientific research examining molecular, cellular, and circuit properties. Acute experiments will involve:

- transcriptomics and epigenomics (tissue from n=12 participants needed for each of epileptic and non-epileptic datasets, in order to acquire sufficient statistical power based upon previously published results)
- whole-cell patch-clamp electrophysiology and morphological reconstructions (n=50 neurons needed for each of epileptic and non-epileptic datasets, likely requiring tissue from ~10 participants, in order to acquire sufficient statistical power based upon previously published results)

There are 22 participants currently enrolled in this study. 1 was enrolled this quarter.

6. **A Placebo-Controlled Efficacy in iNPH Shunting (PENS) Trial:**
   PI: Dr. Thomas Zwimpfer

Funding	Source	Study period	Anticipated Enrolment at VGH Site	# of subjects enrolled	Approval	Status	Abstract/Paper/ Manuscript
Yes	National Institutes of Health	Nov 2022 - Jan 2028	10	1	Yes	Active	N/A

Purpose

Although idiopathic normal pressure hydrocephalus (INPH) has been recognized for five decades, barriers still exist in recognition, referral and accurate diagnosis. Hesitance in referring elderly patients for surgical treatment of INPH results from an incomplete understanding of its pathophysiology, controversy over the appropriate diagnostic work up, and a significant concern about the effectiveness and complications of surgical treatment. The lack of consensus regarding tests predicting outcome of surgery in INPH, and the skepticism of INPH in the neurology and neurosurgery communities reflect the limitations of INPH clinical research to support current INPH practices. Convincing proof of shunting effectiveness is likely to increase the number of INPH patients getting adequate treatment. The Placebo-Controlled Effectiveness in INPH Shunting (PENS) trial is a multi- center blinded, randomized, placebo-controlled design investigation of cerebrospinal fluid (CSF) shunt surgery.

Objective

Primary Objective:

The primary objective is the evaluation of CSF shunting in iNPH participants through a randomized comparison of improvement from baseline at three months between active (open

shunt) and placebo-controlled (closed shunt) groups, using the primary endpoint of gait velocity to test the primary hypothesis: the treatment of idiopathic normal pressure hydrocephalus (iNPH) with an open shunt results in improved gait velocity.

Secondary Objectives:

1. Evaluate the effect of shunting on improving gait and balance between active and placebo-controlled groups at three months using the Tinetti assessment
2. Evaluate the effect of shunting on improving global cognition between active and placebo-controlled groups at three months using the total Montreal Cognitive Assessment (MoCA) score
3. Evaluate the effect of shunting on bladder control between active and placebo-controlled groups at three months using the OAB-q sf.

Justification

There are 5 major manufacturers of shunts. Until now the valves were either differential pressure valves or flow-regulated valves and none of them had the ability to be turned off even if clinically indicated. Thus, doing a placebo study of shunts often involved tying a ligature in the shunt catheter with variable results and adding complexity and additional intervention to untie the ligature. With the release of the new Codman Certas Plus 2.0, a virtual off setting is now available to stop flow of CSF through the shunt system unless intracranial pressures exceed 400 mm which has not been documented in participants with iNPH. This shunt would also rapidly enable lowering settings if indicated in the judgement of the treating physician in the placebo arm without necessitating invasive intervention. No other commercially available shunt appropriate for treating NPH offers these features.

There are 100 participants anticipated to be enrolled across 20 sites. 10 participants will be enrolled at the Vancouver site. 0 participants were enrolled in the last quarter.

7. **<u>Patient outcomes of a subtemporal preauricular infratemporal approach with condylar fossa osteotomy for skull base chondrosarcoma resection:</u>**
   PI: Dr. Ryojo Akagami; Co-I's: Seika Taniguchi

Funding	Source	Study period	Anticipated Enrolment	# of subjects enrolled	Approval	Status	Abstract/Paper/ Manuscript
N/A	N/A	Aug 2022 - Jun 2024	50	32	Yes	Active	N/A

Purpose

To the knowledge of the investigators, there is an absence of reviews that synthesize and analyze the health-related quality of life (HRQoL) outcomes of skull base chondrosarcoma patients who have undergone surgical management using this surgical approach. This study aims to fill this gap in the literature and provide greater insight into the HRQoL of chondrosarcoma patients. Findings from this study may guide clinicians in the management and integration of a biopsychosocial approach to patient care.

Objectives

This retrospective chart review aims to:

1. Evaluate the surgical and clinical outcomes of skull base chondrosarcoma resection using a subtemporal preauricular infratemporal approach with condylar fossa osteotomy.
2. Analyze the impacts of skull base chondrosarcoma on overall patient health related quality of life. This would enrich the understanding of the nuanced, biopsychosocial impact of this condition on patient quality of life and potentially guide future long-term patient management.

Research Design

A retrospective chart review of all patients with skull base chondrosarcoma will be first conducted using existing patient data from charts available on Plexia EMR and VGH hospital records/PCIS. Inclusion and exclusion criteria outlined above will be applied to select for retrospective chart analysis. Relevant surgical and clinical parameters that will be collected and reported on will correspond to pre-, peri- and postoperative records (see attached data collection sheet). The SF-36 questionnaire is part of existing postoperative follow up protocol. Answers from these questionnaires will be tabulated and added to the data collected from the retrospective chart review.

There were 0 participants enrolled this last quarter.

8. **<u>Does temporomandibular joint disruption in performing a condylar osteotomy affect postoperative patient quality of life in skull base tumours:</u>**
   PI: Dr. Ryojo Akagami; Co-I's: Seika Taniguchi

Funding	Source	Study period	Anticipated Enrolment	# of subjects enrolled	Approval	Status	Abstract/Paper/ Manuscript
N/A	N/A	Oct 2022 - Jun 2024	50	32	Yes	Active	N/A

Purpose
To date, there remains an absence of reviews that evaluates and synthesizes the oral health-specific quality of life (OHRQoL) following TMJ disruption in the SPI approach to managing chondrosarcomas. Temporomandibular disorders (TMD) are significant public health problems and are the second most common musculoskeletal condition. second to chronic low back pain. The study aims to provide greater insight into the (OHRQoL) of patients with skull-based tumours, namely chondrosarcomas and trigeminal schwannomas.

Objectives
1. Compare the temporomandibular joint specific oral health related quality of life (OHRQoL) between patients who underwent skull base tumor resection (chondrosarcoma or trigeminal schwannoma) with either temporomandibular joint preserving approach or temporomandibular joint disrupting approach as a result of a condylar osteotomy.
2. Evaluate the subtemporal preauricular infratemporal approach for chondrosarcomas in relation to post surgical temporomandibular joint complications and overall OHRQoL.

Research Design
The skull base tumors used for comparison will be chondrosarcomas and trigeminal schwannomas; chondrosarcoma resection typically involves a condylar fossa osteotomy that disrupts the TMJ, whilst trigeminal schwannoma resection approaches do not impact the TMJ. A retrospective chart review of all patients with skull base chondrosarcoma and trigeminal schwannomas will be first conducted using existing patient data from charts available on Plexia EMR and VGH hospital records/PCIS. Inclusion and exclusion criteria outlined above will be applied to select for retrospective chart analysis. Relevant surgical and clinical parameters that will be collected and reported on will correspond to pre-, peri- and postoperative records (see attached data collection sheet). To assess quality of life, the SF-36 and DC/TMD Axis I and Axis II screening protocol will be administered to patients.

There were 0 participants enrolled this last quarter.

9. **A case-control study: comparing long-term quality of life outcomes across different treatment modalities of surgery, radiation, and active surveillance in acoustic neuroma patients (new this quarter):**
   PI: Dr. Ryojo Akagami; Co-I's: Seika Taniguchi

Funding	Source	Study period	Anticipated Enrolment	# of subjects enrolled	Approval	Status	Abstract/Paper/ Manuscript
N/A	N/A	July 2023 - Dec 2024	100	0	In progress	Not started	N/A

Purpose

There is a lack of longitudinal health-related quality of life (HRQoL) outcomes of AN patients between the main three treatment modalities of surgery, stereotactic surgery and active surveillance that are matched for age, gender, and tumor characteristics. This study aims to fill this gap in the literature and investigate whether there are differences in the longitudinal HRQoL outcomes amongst AN patients between treatment modalities whilst limiting the above potential confounding variables. Findings from this study may guide clinicians in the management and integration of a biopsychosocial approach to patient care.

Objectives

- To evaluate the longitudinal surgical and HRQoL outcomes of AN patients between the 3 primary treatment modalities of surgery, stereotactic radiosurgery and active surveillance.
- To compare and contrast the impact of surgery, radiation and active watching in the management of AN on the longitudinal HRQoL of patients.

Research Design

A retrospective chart review of all AN patients will be first conducted using existing patient data from charts available on Plexia EMR and VGH hospital records/PCIS. Patients who have undergone radiotherapy management and meet the inclusion/exclusion criteria will first be identified where by patient demographics, tumor characteristics, clinical symptoms and SF-36 scores will be collected from the charts. Using this, a 1:1 match that satisfies the matched case control criteria will be applied for the remaining surgical and active surveillance group. Once patients that are matched for the various variables, the same data obtained for the radiotherapy group will be collected. The control group will be the age matched Canadian health population SF-36 scores that have been already published.

There are 100 participants anticipated to be enrolled

10. **<u>Aneurysmal Subarachnoid Hemorrhage - Red Blood Cell Transfusion and Outcome (SAHaRA): A Randomized Controlled Trial:</u>**

Funding	Source	Study period	# of subject enrolled	Approvals	Status
Grant	CIHR	2017-2022	29	Yes	Recruitment ongoing

Purpose
We propose a multicenter pragmatic randomized trial in patients with aSAH that will compare the effect of a liberal to a restrictive RBC transfusion strategy on the combined rate of death and severe disability at 12 months.

Hypothesis
We hypothesize that in adult patients suffering from aSAH and anemia, a liberal RBC transfusion strategy as compared to a restrictive RBC transfusion strategy decreases the combined rate of death and severe disability at 12 months (using the modified Rankin Scale)

Justification
Aneurysmal subarachnoid hemorrhage (aSAH) is a devastating illness caused by the spontaneous rupture of an enlarged, weakened artery in the brain. It affects a young population and is a significant cause of premature death and loss of potential life years, similar in magnitude to ischemic stroke. It is a common neurologic reason for intensive care unit (ICU) admission and is associated with a mortality rate of 35% in North America. Less than one third of afflicted patients make a full recovery and 20% of survivors experience significant morbidity and impacts on daily living.

There are 478 participants enrolled across 20 sites. 29 participants have been enrolled in Vancouver

11. **<u>Vancouver Ruptured Aneurysm Database (VRAD)</u>**
PI: Dr. Peter Gooderham; Co-I's: Drs. Haw, Rebchuk, Chang, Redekop, Rizzuto

Funding	Source	Study period	# of subject enrolled	Approvals	Status
None	N/A	2022-2032	60	Approved	Recruitment and Data Collection ongoing

Purpose
The overall purpose of the registry will be to establish and maintain a longitudinal aneurysmal subarachnoid hemorrhage patient event database to investigate clinical management of subarachnoid hemorrhage. Through this data, long term functional outcomes will be characterized.

Objectives
- To describe the demographic and natural history of patients with subarachnoid hemorrhage
- To characterize the presentation, assessment, and treatment of patients with subarachnoid hemorrhage
- To characterize both open surgical and endovascular management for subarachnoid hemorrhage
- To describe hospital-related complications and long-term clinical outcomes for subarachnoid hemorrhage patients

Study Design
This is an observational prospective cohort study. Participants will be recruited by study investigators. They will be flagged upon presentation to hospital and the neurosurgery service. The neurosurgery service is consulted on all cases of suspected aSAH and intracranial aneurysms at Vancouver General Hospital. Data will be extracted from hospital charts and electronic medical records. We will collect basic demographics, past medical history, clinical presentation, treatment, complications, clinical and functional outcomes. Hospital and clinical data will be collected and stored in an online web-based registry constructed using UBC ARC REDCap.
There are 60 participants enrolled from Vancouver General Hospital. 32 participants have been enrolled in the last quarter.

12. **<u>The SmartForceps System: An Intelligent Device for Real-time Measurement of Forces of Tool-tissue Interaction during Surgery, towards Assessment of Surgical Skill and Performance:</u>**

PI: Dr. Serge Makarenko
Co-I: Dr. Peter Gooderham

Funding	Source	Study period	# of subject enrolled	Approvals	Status
Grant	CIHR	2022	0	REB approved. Pending VCHRI Approval.	Awaiting equipment arrival

Purpose
This study aims to trial SmartForceps, a new tool that is the first of its kind, integrated with force sensors for real-time sensing and monitoring of coagulation, dissection and tool-interaction forces during surgery. This includes a force monitoring system, allowing the ability to monitor and record surgical forces during procedure, providing helpful feedback to surgeons.

Hypothesis
1. The SmartForceps System will differentiate surgeons by their skill level
2. Surgical task specific force profile will be automatically and reliably recognized and created by the machine-learning module.
3. Shortened operating room time in comparison to historical controls.

Justification
It has been shown using virtual reality simulators that ~50% of surgical errors are related to the use of inappropriate/excessive force. Currently, the ability to apply optimal force during tool-tissue interaction in surgery is only mastered through years of hands-on surgical training. This knowledge remains largely qualitative, as none of the commercially available surgical instruments provide real-time measurement of intra-operative surgical forces. When a surgeon is operating or supervising a trainee, there is no objective means of evaluating the amount of force applied, and trauma to delicate tissues such as brain or nerve tissues often cannot be detected until obvious injuries have occurred.

The SmartForceps is the first of its kind, integrated with force sensors for real-time sensing and monitoring of coagulation, dissection and tool-interaction forces during surgery. The prototype

included a calibration station, signal conditioning and filtering module, together with a force monitoring system, allowing the ability to monitor and record surgical forces during procedure.

13. **Subarachnoid Hemorrhage - Vasospasm Neuromonitoring**
PI: Dr. Peter Gooderham; Co-I's: Drs. Griesdale, Rebchuk, Sekhon

Funding	Source	Study period	# of subject enrolled	Approvals	Status
None	N/A	2022	0	Approved	Recruitment and Data Collection

Purpose
Currently, detection of delayed cerebral ischemia in patients presenting with subarachnoid hemorrhage is undertaken by scans or clinical exams, which have limitations. This study will assess whether specialized micro-catheter monitors that are inserted into the brain following aneurysmal subarachnoid hemorrhage can allow for early detection of delayed cerebral ischemia.

Objectives
- To examine differences in PbtO2 in aneurysmal subarachnoid hemorrhage (aSAH) patients with delayed cerebral ischemia (DCI) vs those without
- To examine differences in cerebral blood flow in aSAH patients with DCI vs those without
- To examine differences in lactate/pyruvate ratio in aSAH patients with DCI vs those without
- To examine differences in SjvO2 in aSAH patients with DCI vs those without
- To correlate PbtO2, cerebral blood flow, lactate/pyruvate ratios during DCI to functional and quality of life outcomes at discharge, 6 months, 12 months, and 2 years post-ictus

Study Design
This is a prospective interventional study. Participants will be screened and recruited by study investigators and research assistants. They will be flagged upon presentation to hospital and the neurosurgery service. An intraparenchymal catheter will be placed within the sub-cortical white matter of participants to real-time monitoring and assessment of key information such as brain oxygenation, cerebral blood flow, cerebral metabolism, and exchange of oxygen in the cerebral vascular bed. This will allow us to directly explore how the cerebral microvascular changes in response to vasospasm and in patients that develop delayed cerebral ischemia.

14. **Prospective registry for adults with Moyamoya disease and Moyamoya syndrome at the Vancouver Stroke Program**

PI: Dr. Yip; Co-PI: Drs. Gooderham, Sheldon, Teal

Funding	Source	Study period	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
No	n/a	2023-2027	9	Yes	Approved	N/A

Background

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 purpose of this registry is to improve our understanding of the natural history and outcomes of patients living with Moyamoya disease and Moyamoya vasculopathy.

There is currently no curative treatment for Moyamoya, however some interventions exist to reduce the risk of ischemic and hemorrhagic complications as well as the onset of other symptoms. Although these interventions are available, there is a lack of consistent information regarding the demographics and natural history of this patient population, and importantly, their long-term outcomes. This registry will allow us to prospectively assess this patient population overtime which is essential for improved understanding, and treatment, of this rare disease.

8 participants were enrolled in the last quarter.

15. **<u>Moyamoya disease in Indigenous Populations in British Columbia: Presentation, treatment, outcomes, and specific challenges they face</u>**

PI: Dr. Gooderham; Co-PI: Drs. Yip, Teal, Hounjet

Funding	Source	Study period	# of subjects enrolled	Approvals	Status	Abstract/Paper/Manuscript
No	n/a	2023-2024	n/a	n/a	Pending CREB Approval	N/A

Background

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. This disease has been well-characterized in the literature among Korean and Japanese populations. Clinically, there appears to be a disproportionate representation of Indigenous peoples affected by this disease in British Columbia, but this has not been documented in literature.

Objectives

This study aims to provide a clinical and radiographic description of Moyamoya disease among Indigenous people in British Columbia, while also assessing data on barriers to care and recovery. With an eye to future research, patients will be asked to identify, as they are comfortable and able, potential avenues to future contact with their community for collaborative research regarding traditional knowledge and stories that may pertain to stroke-like presentations in young people.

3. ONGOING RETROSPECTIVE STUDIES

1. **Wounded Glioma Syndrome: neurologic worsening in patients with Subtotal Resection in High-Grade Gliomas**

PI: Dr. Serge Makarenko
Co-I: Dr. Michael Rizzuto, Crystal Ma (Year 2 Medical Student)

Study period	Approvals UBC CREB/VCHRI	Anticipated number of patients reviewed	Status	Abstract/Paper /Manuscript	Funding
Jan 2000 - Dec 2021	Approved	200	Data Collection	N/A	N/A

Purpose
First line treatment for high-grade gliomas is surgery with goals of maximally safe resection, and subsequent radiation and chemotherapy. Surgery serves other purposes aside from removing the malignancy, it alleviates the raised intracranial pressure through reduction of mass effect, and additional cytoreduction. A greater extent of resection generally results in better survival for patients with high-grade gliomas. Although the ideal treatment for high-grade gliomas is gross total resection, this approach is not always feasible owing to the infiltrative quality of these tumors. Moreover, neurosurgeons may choose to pursue a relatively more conservative approach such as subtotal resection rather than gross-total resection to minimize injury to eloquent areas that are important for overall quality of life and survival. A delicate balance is presented to the neurosurgeon, achieving maximal resection in order to improve and prolong survival, while balancing it against morbidity and preserving quality of life. One of the challenges with subtotal resection in the early post operative period, is that the residual tumour tissue can lead to associated morbidity in the form of post-operative edema and swelling, and worsening neurologic function. Our aim is to investigate if tumor remaining at the surgical site after subtotal resection entails post-operative neurological injury and deficit, whether this may be due to inflammation or another physiological process.

Hypothesis
We hypothesize that patients with high-grade gliomas who have undergone subtotal resections will experience an increased risk of post-operative neurological worsening within the first 7-10 days post-operatively.

Justification

High-grade gliomas are common and devastating brain malignancies for which surgery is the first-line treatment. Subtotal resections result in residual tumor that may be associated with neurological worsening and other post-operative complications. Our aim is to whether subtotal resections result in immediate post-operative neurological deficits, specifically 7-10 days after surgery, identify associated factors, characterize other complications, and report an ideal threshold for resection that minimizes neurological deficits. We anticipate these findings will further our understanding of improving surgical outcomes to optimize patient quality of life. Furthermore, by helping delineate the safest extent of resection, we hope to provide additional guidance for surgeons in decision-making around resection of these tumours.

2. **Recurrence in WHO Grade 1 meningiomas – is there a pattern of clustering among recurrent Grade 1 meningiomas that could help target radiation therapy?**

PI: Dr. Serge Makarenko
Co-I: Dr. Michael Rizzuto

Study period	Approvals UBC CREB/VCHRI	Anticipated number of patients reviewed	Status	Abstract/Paper /Manuscript	Funding
Jan 2000 - Dec 2021	Approved	1078	Data Collection	N/A	N/A

Purpose
We aim to elucidate the pattern and location of tumor recurrence to target radiation therapies for recurrent Grade 1 meningiomas

Hypothesis
We hypothesize that there will be a pattern of geographic and temporal clustering of recurrence in WHO Grade 1 meningiomas that can allow for targeted adjuvant radiotherapy delivery.

Justification
Meningiomas are common neoplasms in the population that may lead to morbidity and potential mortality. While the current literature suggests that certain patient and tumor specific factors (including patient sex, type and grade of meningioma, and molecular signature) can predict recurrence, the efficacy of adjuvant RT in preventing and managing recurrent disease is not well characterized. Additionally, determining geographic patterns of tumor recurrence is important in aiding the delivery of RT in patients with recurrent disease. Understanding when, where and how

RT should be delivered in patients diagnosed with WHO Grade 1 meningiomas will allow for a tailored approach to therapy based on geographic location of the initial tumor and recurrence.

3. A Retrospective Review of Treatment Outcomes for Glioblastoma Patients across British Columbia

PI: Dr. Mostafa Fatehi
Co-I: Dr. Michael Rizzuto

Study period	Approvals UBC CREB/VCHRI	Anticipated number of patients reviewed	Status	Abstract/Paper /Manuscript	Funding
Mar 2023 - Aug 2024	UBC CREB Approved Awaiting VCHRI Approval	300	Awaiting VCHRI Approval	N/A	Grant

Purpose
To establish overall and median survival of a current cohort of patients treated for glioblastoma in BC undergoing standard treatment algorithms

Hypothesis
This study will validate the predicted improvement in glioblastoma outcome against actual practice results for the time period of 2016-2022

Justification
This study will serve to document whether patients in BC are experiencing improvements in survival predicted by recent literature reports. DEviance or improvements on these predictions will be surveyed to qualitatively ascertain causation. The actual performance of local treatment strategies must be audited and insurances made that real world results meet expectations.

4. **Utility of Cerebral Angiography in Identifying Cerebrovascular Pathology in CTA-Negative Subarachnoid Hemorrhage (new this quarter)**

PI: Dr. Mostafa Fatehi
Co-I: Dr. Michael Rizzuto

Study period	Approvals UBC CREB/VCHRI	Anticipated number of patients reviewed	Status	Abstract/Paper /Manuscript	Funding
Mar 2023 - Aug 2024	Approved	200	Data collection	N/A	N/A

Purpose
To document how often a DSA study reveals actional pathology in patients with a CTA-negative subarachnoid hemorrhage, and how often this information results in change of management at Vancouver General Hospital.

Hypothesis
DSA will reveal actionable cerebrovascular pathology to a greater extent than repeat or delayed CTA in patients presenting initially with a CTA-negative subarachnoid hemorrhage, and no cerebrovascular pathology on index CTA.

Justification

There would be clinical utility in understanding how often a DSA identifies a vascular pathology and thus alters the management of a patient. It would help better understand what tests and interventions may be applicable for patients with CTA negative SAH and could be used to better guide the diagnostic management of these patients. Ultimately, this may potentially decrease the risk to patients through unnecessary diagnostic testing, improving their management and workup.

5. **Milrinone for the Perioperative Management of Cerebral Hypoperfusion Complicating Moyamoya Syndrome and Moyamoya Disease (new this quarter)**

PI: Dr. Peter Gooderham
Co-I: Christy Richards (Year 2 Medical Student)

Study period	Approvals UBC CREB/VCHRI	Anticipated number of patients reviewed	Status	Abstract/Paper /Manuscript	Funding
Jun 2023- Aug 2023	Approved	200	Data collection	N/A	N/A

Purpose
To investigate the efficacy of milrinone in alleviating hypoperfusion complications of Moyamoya disease

Hypothesis
There will be significant improvement of neurological outcomes in the patient cohort that is administered milrinone intraoperatively, as compared to postoperatively.

Justification

Moyamoya is a rare cerebrovascular disorder that is associated in cerebrohypoperfusion, manifesting in ischemic stroke events or transient ischemic attacks, which can result in permanent neurological deficits. The efficacy of milrinone in managing complications of Moyamoya is not documented in the literature. We aim to document the degree of resolution of perioperative complications for surgical revascularization in Moyamoya performed at VGH, to better understand the efficacy of milrinone and optimal timing of administration

4. INACTIVE OR COMPLETE STUDIES

1. **Survival and Recurrence Outcomes Following Adjuvant Radiotherapy for Grade 2 Intracranial Meningiomas: 13 year Experience in Tertiary-Care Centre**

PI: Dr. Serge Makarenko
Co-I: Dr. Alex Rebchuk

Study period	Approvals UBC CREB/VCHRI	Anticipated number of patients reviewed	Status	Abstract/Paper /Manuscript	Funding
Oct 2007 - Oct 2021	Approved	189	Complete	Published	N/A

Purpose of research

In this study, we will explore whether adjuvant radiation therapy (RT) provides overall survival (OS) and progression-free survival (PFS) benefit following resection of grade II meningioma in our local cohort. We will perform subgroup analysis to compare whether the extent of resection and timing of RT have a modifying effect on OS and PFS in this cohort. We also hope with subgroup analysis, to clarify if specific pathologic features of atypical meningiomas affect outcomes. Furthermore, we will explore whether the 2016 diagnostic change to grade II meningioma has affected the prevalence rate of these diagnoses. These results will guide local practice patterns in patients with grade II meningiomas.

Research Aims

1) Explore whether adjuvant RT following operative resection of grade II meningioma has an effect on PFS and OS
    a) Explore any modifying effect by Simpson grade (Grade 1 v Grade 2-3)
    b) Explore any modifying effect of RT timing (early [<6wks] v late [>6wks])
2) Determine whether grade of resection predicts OS or PFS in grade II meningiomas
3) Explore clinical and histopathological predictors of OS and PFS, and tumour recurrence in grade II meningiomas
4) Explore whether recent changes to histopatholgoical diagnosis of meningiomas has affected prevalence rate
5) If possible, explore the effect of watch and wait versus operative +/- RT treatment for asymptomatic grade II meningiomas

Design

We will perform a single center retrospective chart review. Patient level data will be obtained from Vancouver General Hospital and BC Cancer Agency database between October 2007 and December 2020.

Published in World Neurosurgery May 2022 Edition