Report on Research Activities in the Pediatric Neurosurgery Program

July 1st, 2023 to December 31st, 2023

Prepared by

Annika Weir
Clinical Research Coordinator
Division of Neurosurgery
BC Children's Hospital
University of British Columbia

Reviewed by

Dr. Vesna Popovska
Neuroscience Research Director
BC Children's Hospital

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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 Coordinator (CRC) of the University of British Columbia's (UBC's) Division of Neurosurgery at BC Children's Hospital for the period of July 1, 2023 to December 31, 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 CRC. The studies that are supported by the CRC in this report are divided into three categories of studies: prospective studies, retrospective studies, and inactive/completed studies. The number of studies per category is presented in the table below.

Number of Ongoing Studies			
Prospective	Retrospective	Inactive/ Completed Studies	Total
8	5 (1 new)	2	15

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

2. ONGOING PROSPECTIVE STUDIES

1. **HCRN ESTHI** – Endoscopic versus Shunt Treatment of Hydrocephalus in Infants

Site PI: Dr. Mandeep Tamber; Co-PI: Dr. Ash Singhal, Dr. Faizal Haji

Funding	Source	Amount	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	NIH - NINDS	$140,273	2020-2025	176 in 14 centres; 4 @ BCCH	2	Yes	Active	N/A

Hydrocephalus is commonly treated with the placement of a shunt. Another treatment is endoscopic third ventriculostomy with choroid plexus cauterization (ETV+CPC). This study aims to determine if there are any differences in long term outcomes between shunt and ETV+CPC on brain function. Both of these surgical procedures are standard and are commonly performed by pediatric neurosurgeons; neither one is experimental. Enrolled patients will have neurocognitive testing done before and after, questionnaires will be administered to assess the patient's progress, CSF samples will be collected during the operation, and follow-up data will be collected.

The purpose of this study is to conduct a prospective randomized control trial to compare intellectual outcome and brain structural integrity between 2 hydrocephalus treatments (shunt or ETV+CPC), to help families make the best treatment decision for their baby. The Primary Hypothesis of this study is that a strategy of initial treatment of hydrocephalus with ETV+CPC will result in 12-month cognitive outcome, as assessed by Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III), that is not inferior to cognitive outcome achieved with initial treatment with shunt, among infants eligible for either procedure. Non-inferiority is defined as rejection of the null hypothesis that 12-month Bayley-III Cognitive Scale score is at least 1.5 points lower among infants randomized to ETV+CPC versus those randomized to shunt. This is a multicentre study being carried out by the HCRN. Dr. Tamber is the Site PI at BCCH and Dr. John Kestle is the study PI.

The study is open to enrolment. There were no enrolments in the last 6 month period.

2. **HCRN Registry** – Characterizing Patient Populations in the Hydrocephalus Clinical Research network (HCRN)

Site PI: Dr. Mandeep Tamber; Co-PI: Dr. Paul Steinbok, Dr. Ash Singhal, Dr. Faizal Haji

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	2014-present	All eligible	297	Yes	Active	N/A

The Hydrocephalus Clinical Research Network (HCRN) has been established by philanthropic funding to conduct multi-institutional research (clinical trials and observational studies) on pediatric hydrocephalus. The HCRN Core Data Project has been developed to obtain data about

all neurosurgical hydrocephalus events from the network Clinical Centers, and to create a database to be used by HCRN investigators. The ongoing maintenance of the Core Data Project serves two main purposes: (1) it will help investigators understand the variability, progression, and current treatment practices for hydrocephalus in children, with an ultimate goal of better guiding and assessing therapeutic intervention and providing recommendations on patient care and; (2) it will provide pilot and descriptive data necessary for hypothesis generation and study design (i.e. preliminary power analyses, recruitment projections) for studies under development by the HCRN. This multi-institutional database will be maintained throughout the lifetime of the HCRN, and may be useful for tracking trends in pediatric hydrocephalus over time.

There are 297 subjects included in the registry from BCCH. Thirty one new subjects were included in the last 6 months.

3. **<u>CSF Shunt Infection Study</u> – Novel Biomarker Investigation for Patients Undergoing CSF Shunt Infection Treatment**

Site PI: Dr. Mandeep Tamber; Co-PI: Dr. Ash Singhal, Dr. Faizal Haji

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	NIH	2024-2032	300 @ BCCH	144	Yes	On hold until funding is renewed	N/A

The primary objective of this prospective observational study is to investigate the utility of several novel biomarkers in the management and treatment of CSF shunt infection with a focus on quantitative 16S rRNA PCR amplification, high throughput sequencing of CSF, and microscopy of hardware. We will obtain samples relevant to the investigation of CSF shunt infection, including the CSF shunt apparatus that was removed as well as additional CSF over the course of treatment for CSF shunt infection. We will determine how several proposed biomarkers can inform management and treatment of CSF shunt infection. In addition, CSF and shunt samples will be collected from patients undergoing temporizing hydrocephalus surgeries, initial CSF shunt placement, and CSF shunt revision or removal both as negative controls and to understand the evolution of the biomarkers prior to development of CSF shunt infection. This data will be supplemented with clinical data obtained from chart review. Biological samples not used immediately in this study will be banked for future studies of CSF shunt infections.

There are 144 subjects enrolled into the study. Grant has been submitted and now waiting on funding decision.

4. **<u>Craniosynostosis Training and Assessment Study</u>**

PI: Dr. Faizal Haji; Co-PI: Dr. Erika Henkelman, Dr. Mandeep Tamber, Dr. Ash Singhal, Dr. Douglas Courtemanche, Dr. Saoussen Salhi, John Jacob

Funding	Source	Study period	Anticipated enrolment	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	Dept. of Surgery Seed Grant	2022-2024	N/A – QI/QA study	Approved	Active	N/A

Craniosynostosis is a condition where the bones in an infant's skull prematurely fuse leading to skull shape abnormalities. Traditionally, the diagnosis and management of craniosynostosis is taught using lectures, textbooks, and clinical encounters with infants presenting in clinic. However, the relative rarity of craniosynostosis limits the clinical exposure required to develop the diagnostic skills. Given the ubiquity of mobile devices and internet access, e-learning may provide a teaching method with the potential to fill this educational gap. The purpose of this study is to develop and evaluate a multimodal e-learning course with interactive 3D virtual models for teaching.

The tool is currently being drafted and the assessment is being created. Once complete, the tool/assessment will be sent out to learners.

5. Learning Engagement in Simulation Study

PI: Dr. Faizal Haji Co-I: Isabella Watson

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
Yes	CAME Foundation	2022-2024	20	0	Approved	Active	N/A

More research is needed on context specificity of learner engagement and the unique features of simulated learning environments in health professions. This study aims to explore engagement during simulation-based education through conducting interviews with learners and instructors. The main goal is to determine what factors learners and instructors believe support learner engagement, as well as how to identify an engaged learner. Participants will be recruited from simulation courses and semi-structured interviews with simulation instructors and learners will be conducted. Data from observational field notes and interviews will be analysed in order to gain a better understand of learner engagement in simulations.

REB application has been approved. Study is being conducted at Queen's University. There are no enrolments in the last term.

6. Spinal Cord Clinic Database

PI: Dr. Soojin Kim; Co-I: Dr. Faizal Haji, Dr. Andrew MacNeily, Dr. Anne Jekyll, Deeya Bhardwaj, Dr. Christine Alvarez, Dr. Elizabeth Grant, Dr. Jacqueline Purtzki, Dr. Soojin Kim, Jennifer Louie, Louise Byron, Olivia Ryder, Dr. Rajiv Reebye, Dr. Sarah Courtice, Zoe Schwartz, Zoe Schwartz, Sophie Hopkins, Dr. Thomas de Los Reyes

Funding	Source	Study period	Anticipated enrolment	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	2020-2025	N/A – QI/QA study	Approved	Active	N/A

The Spinal Cord Clinic is a multidisciplinary clinic at British Columbia Children's Hospital (BCCH), Royal Columbian Hospital, and New Westminster Rehabilitation Medicine. At the BCCH clinic, patients with spinal cord abnormalities are seen by a wide range of specialties including: orthopaedics, urology, social work, paediatrics, neurosurgery, and physical therapy. As a quality improvement initiative, this study aims to create a longitudinal database for the Spinal Cord Clinic at BC Children's Hospital to assess patient-reported quality of life, transition readiness, mental health, physical activity level, and health literacy.

Data collection is ongoing for the database.

7. Canadian Epilepsy Surgery Registry

PI: Dr. Mandeep Tamber; Co-Is: Dr. Mary Connolly, Dr. Faizal Haji, Dr. Ash Singhal, Dr. Cyrus Boelman, Dr. Anita Datta, Dr. Linda Huh

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status
Yes	BCCHRI Establishment Award	2000 - present	All eligible	0	Yes	Approved

The Department of Neurosurgery at BCCH is working to develop a Canada-wide population-based registry for pediatric patients undergoing epilepsy surgery. The goal of this registry is to improve population health and health system sustainability by: 1) accelerating accumulation and efficient sharing of best practice knowledge; 2) enabling provincial/national health systems planning through population-based health data analytics; 3) providing hospital performance measures to drive quality improvement; and 4) creating nimble health technology assessment capacity for innovative yet unproven therapies as they develop. This multi-institutional retrospective and prospective database will be maintained indefinitely and may be useful for tracking trends in pediatric epilepsy surgery over time.

Study has been approved by REB and a Canadian epilepsy surgery conference is being planned.

8. Factors That Influence Surgeons' Use of Knowledge Translation Tools in HCRN and HCRNq

PI: Dr. Mandeep Tamber; Co-Is: Dr. John Kestle (University of Utah)

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status
No	N/A	2023 - 2024	~160	0	Yes	Approved

The HCRN is a network composed of hospitals across Canada and the USA dedicated to researching pediatric hydrocephalus. This network generates research-based instruments and

protocols to help improve the diagnosis, treatment, and outcomes of hydrocephalus patients. However, it is not known whether this evidence-based medicine (EBM) is being implemented by sites outside the HCRN and whether surgeons' attitudes, beliefs and knowledge related to EBM may lead to differences in their behaviour towards new information and ultimately how EBM is applied clinically. The purpose of this study is to explore the relationship between EBM-related attitudes, knowledge and behaviours of pediatric neurosurgeons and their utilization of evidence-based knowledge translation instruments relevant to the treatment of pediatric hydrocephalus. A survey will be sent out to all surgeons in the HCRN and HCRNq (approx. 160 surgeons) to determine surgeon characteristics that may affect knowledge application to ultimately help better tailor future instruments/protocols to pediatric neurosurgeons.

The study has been approved and the survey is being created.

3. ONGOING RETROSPECTIVE STUDIES

1. Endo-Sag Cephalic Index Study

PI: Dr. Ash Singhal; Co-I: Dr. Mandeep Tamber, Dr. Faizal Haji, Isabella Watson

Funding	Source	Study period	Approval	Charts Reviewed	Status	Abstract/Paper/ Manuscript
No	N/A	2022-2024	Yes	72	Active	Submitted

Craniosynostosis is a condition where one or more sutures of the skull fuse pre-maturely. Sagittal synostosis is the most common form of single-suture synostosis making up 40-60% of all craniosynostosis cases. The cephalic index (CI) is particularly useful in cases of sagittal synostoses. Research has been done on the timing of open cranial vault reconstructive surgery but less is known about optimal timing and long term CI outcome in endoscopic suturectomies. With cranial vault surgeries it has been found that earlier intervention leads to a better post-operative CI in the long term. There is scarce literature that analyzes the change in cephalic index using multiple, more frequent data points post-operatively, particularly in endoscopic suturectomies. With more frequent measurements of CI, trends may surface that would normally be missed and more knowledge may be gained on operative technique, cosmetic outcome, and orthotic use.

The purpose of this study is to investigate the longitudinal change in cephalic index to determine if there are any underlying trends and an optimal age for surgical intervention. With this study, we hope to gain more insight into the care of sagittal synostosis patients who have been treated by endoscopic-assisted surgery.

This study had its manuscript submitted. Further data collection and analysis is ongoing to expand the study for a future second publication.

2. Spinal Ultrasound Study

PI: Dr. Mandeep Tamber

Study period	Approval	Charts Reviewed	Status	Abstract/Paper/ Manuscript	Funding
2021-2023	Approved	442	Active	N/A	N/A

Primary spinal anomalies are a broad group of developmental malformations of the spine and its surrounding tissues. These include the spinal dysraphisms, a series of malformations caused by inappropriate development of the neural tube or its overlying ectodermal layers, tethered cord syndromes, or split cord malformations. These disorders range from being asymptomatic to having severe motor, bowel/bladder, and musculoskeletal manifestations in children and young adults. Some spinal anomalies are associated with cutaneous manifestations visible on the lower back, such as a tuft of hair, hemangioma, skin tag, or sacral dimple. As such, routine physical examination of all newborn babies includes an assessment for these findings. Patients with concerning physical exam findings often are referred for lumbosacral imaging to rule out a spinal anomaly. It has been our anecdotal experience that many primary care physicians continue to order ultrasound imaging to investigate simple dimples in neonates, despite clinical practice recommendations against them, causing unnecessary cost and utility of resources.

We hypothesize that current use of ultrasound in children for workup of suspected spinal anomaly is inappropriately over-utilized. The purpose of this study is to assess the current landscape of ultrasounds performed for investigation of spinal anomalies in babies with ultrasound. The potential impact is that considerable cost savings to our healthcare budget may result from this quality assurance initiative.

Data collection is complete – data analysis and manuscript write up underway.

3. **Surgical Management of Pineal Region Tumors**

   PI: Dr. Ash Singhal; Co-I: Dr. Julian Zipfel-***new study this term***

Funding	Source	Study period	Approval	Charts Reviewed	Status	Abstract/ Paper/ Manuscript
No	N/A	2023-2025	Yes	31	Active	N/A

Tumors of the pineal region are rare in the pediatric population and are associated with significant morbidity and mortality. Primary symptoms often arise due to obstructive hydrocephalus caused by aqueductal obstruction. Consequently, headaches and general signs of increased intracranial pressure (ICP) are common symptoms but also visual impairment. The encountered pathologies and thus the management of patients with pineal region tumors are diverse. Often, symptomatic obstructive hydrocephalus has to be treated surgically, sometimes combined with biopsy via neuroendoscopy if blood and cerebrospinal fluid tests are inconclusive. The pineal region is surrounded by critical neurovascular structures. Symptoms, pathologies, their general treatment protocols and the surgical approaches employed in the case of resection are very diverse. By comparing pineal region histologically differentiated tumor types, molecular pathological results, and surgical approaches, we wish to generate data on these rare lesions and help to better understand clinical management. Furthermore assessing the individual course of Optic Nerve Sheath Diameter in pre- and postoperative imaging may help give insight into ICP-dynamics during treatment.

This study is undergoing data collection.

4. **Unintentional Falls Study**:

   PI: Dr. Ash Singhal; Co-PI: Dr. Mandeep Tamber, Dr. Stephano Chang, Dr. Ruth Mitchell, Alexander Cheong

Study period	Approval	Charts Reviewed	Status	Abstract/Paper/ Manuscript	Funding
2021-2023	Approved	816	Active	N/A	N/A

Unintentional falls are the leading cause of non-fatal injuries in the pediatric population, with falls representing one of the most common reasons for emergency department visits. Children under the age of 5 are particularly vulnerable to falls from windows and balconies, which result in serious injuries and are largely preventable. Public health initiatives such as community education and installation of window guards in several cities have successfully decreased the incidence of window falls among children - one such initiative, a city health code mandating

window guards where children 10 years or younger live, resulted in a 96% decrease in the incidence of unintentional window falls. In addition to the prevention of numerous serious injuries, these relatively low-cost solutions would likely free up significant healthcare and community resources required to treat these patients.

The pediatric population in the province of BC remains theoretically vulnerable to these preventable falls from windows due to our current provincial building code. Understanding the local epidemiological patterns of unintentional falls and trauma are essential to determining the most appropriate and likely-to-be-effective interventions. We are interested in retrospectively accessing the BCCH trauma database to understand the demographics, specific circumstances, and treatments for patients involved in unintentional falls from windows over the past 20 years.

Additional data collection and secondary data analysis underway.

5. Pediatric Intracranial Infection Complicating Bacterial Sinusitis in Canada

PI: Dr. Mandeep Tamber; Co-Is: Dr. Faizal Haji, Dr. Ash Singhal

Funding	Source	Study period	Approval	Charts Reviewed	Status	Abstract/ Paper/ Manuscript
No	N/A	2023 - 2024	Yes	43	Active	N/A

Intracranial infections can arise as a complication of sinusitis, usually caused by Streptococcus bacteria. These infections encompass brain abscesses, and empyemas, which are collections of purulent exudates (pus). Intracranial infective complications are relatively rare in the pediatric population; however, they pose a significantly high morbidity/mortality risk. Furthermore, patients, who survive the infections, typically endure lengthy hospitalizations and urgent surgical management, along with devastating long-term neurological outcomes. Neurosurgeons at BC Children's Hospital and at other Canadian pediatric neurosurgical centers have anecdotally noted that intracranial infective complications of bacterial sinusitis have been trending upward since the onset of the COVID-19 pandemic in 2020. However, detailed current Canadian data on the intracranial complications of sinusitis in children is lacking. The objective of this study is to ascertain the epidemiology of pediatric intracranial infections, particularly those caused by Streptococcus bacteria, occurring as a consequence of bacterial sinusitis, from 2016 to 2022 and to investigate the proportion of negative outcomes before and after the onset of the COVID-19 pandemic.

REB application has been approved. Data entry and data analysis at BCCH is complete. Other sites across Canada are currently submitting their own respective REB applications.

4. INACTIVE OR COMPLETE STUDIES

1. **RoR and Neurosurgical Adverse Events Study**

PI: Dr. Ash Singhal; Co-I: Hana Miller

Funding	Source	Study period	Approval	Charts Reviewed	Status	Abstract/ Paper/ Manuscript
No	N/A	2023	Yes	3849	Completed	Abstract completed

Access to healthcare in Canada is rooted in the values of fairness and equity. In the past decade, discussions regarding whether or not data supports these values have increased dramatically. As our country becomes more aware of the barriers to care different populations might face, it is imperative that we consider geography as part of the socio-exposome. The vast geographic expanse of the country presents challenges to delivering specialized care to remote and rural communities. This is particularly true for pediatric patients living far from specialized pediatric health-care centers who require specialized surgical interventions. The impact of RoR on surgical outcomes is being increasingly studied in adult populations, but limited research exists on the impact of RoR on pediatric surgical outcomes. The goal of the project will be to examine the association that remoteness of residence (RoR) has on pediatric surgical outcomes in British Columbia. Outcomes will be defined by readmissions, surgical site infections, and other adverse events as indicated by NSQUIP data.

The study's abstract has been completed and manuscript writeup is underway.

2. **Spatiotemporal Mapping and Decoding Oculomotion Functions in the Frontal Eye Fields**:

PI: Dr. Ash Singhal; Co-PI: Dr. Mandeep Tamber, Dr. Stephano Chang, Dr. Faizal Haji, Alexander Cheong

Funding	Source	Study period	Anticipated enrolment	# of subjects enrolled	Approvals	Status	Abstract/ Paper/ Manuscript
No	N/A	2021-2023	10	13	Approved	Active	N/A

The frontal eye field, often described as an important control area, located on a specific part of the brain in the prefrontal cortex. However, the exact localization and function of this area are still debated. A study of functional localization of this region in pediatric population does not exist and may help understand the development of eye function in humans, making epilepsy surgery safer for this population. As a part of normal standard of care, patients would be monitored using electrodes implanted on their brain. We propose to collect additional eye movement data during this period.

Study no longer enrolling participants. Data analysis and manuscript is currently underway.