Faculty of Medicine, Office of Research

Faculty of Medicine Multidisciplinary Research Program in Medicine Evaluation Report

2022 Program

THE UNIVERSITY OF BRITISH COLUMBIA

Faculty of Medicine Multidisciplinary Research Program in Medicine Evaluation Report

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for Faculty of Medicine Office of Research

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Program Overview

Program Description

The Faculty of Medicine Multidisciplinary Research Program in Medicine (FoM MRPM) provides undergraduate students with an opportunity to explore their interest in interdisciplinary and multidisciplinary research by undertaking a summer project supervised by a cross-faculty pair of researchers based on the success of the University of British Columbia at Okanagan's Multidisciplinary Undergraduate Research Projects in Health (MURPH) program.

"It is extremely helpful to have students involved with our research. They provide the energy, talent and extra hands need in our labor-intensive research. Students are motivated and excited to be part of our research lab, and that enthusiasm is infectious— It makes us all want to do more to solve our research questions."

-MRPM Supervisor

The goal of the program is to pair researchers across faculties with undergraduate and MD students for the purposes of conducting multidisciplinary/interdisciplinary research. With this goal in mind, successful primary supervisors from the Faculty of Medicine (FoM) and co-supervisors from across UBC are matched with two non-MD undergraduate students and an optional MD student for their research project (see Figure 1 for co-supervisor disciplines). Undergraduate and MD students conducted 16- or 8-weeks of full-time research, respectively over the summer of 2022. A Postgraduate Student Advisor was assigned by the supervisors to spearhead training and oversight on the project and gain valuable supervisory experience.

Objectives

Given the excellent feedback received from the 2021 FoM MRPM pilot program, we expanded the 2022 FoM MRPM program and made the process more inclusive. As with our 2021 objectives, this program primarily aims to provide unique funding opportunities to collaborate across disciplines, in-line with overall FoM strategic plan, and to provide training and professional development to UBC undergraduate students. Specifically, these student learning objectives include:

- Networking and collaborating with supervisors and students across typically siloed disciplines
- Fostering scientific communication skills including opportunities to give a research conference presentation
- Developing concrete research skills that will have a meaningful impact on future student success and further important research goals

To make the application process more inclusive, we included an additional stream for underrepresented students. To do so we asked students to self-identify as an Indigenous student or a as a student with a disability. Those that self-identified in one of those two groups were automatically entered to receive an award for full funding from the FoM in line with our commitment to Equity, Diversity, and Inclusion principles and in partnership with the Indigenous Strategic Plan.

Approach

"It was a great opportunity to have subsidized studentships. The undergraduate students were able to actually do the experiments that allowed us to explore a new research collaboration."

- MRPM Supervisor

Application Process

Supervisors and students applied for the MRPM program separately with staggered deadlines. Supervisors first submitted project applications by February 18th, 2022. Supervisor applications required a FoM-appointed primary supervisor to collaborate with a non-FoM co-supervisor and choose a postgraduate student advisor to help supervise the project. Along with contact details, supervisors were required to write a project summary and benefit to the student statement for review. These statements were packaged and sent for adjudication to a panel of researchers to score (see Table 1 for adjudicator scoresheet). Project applications were ranked based on adjudicator scores and the top projects were chosen for funding. In this case, all 16 eligible projects were funded for the summer 2022 round (see Table 2 for application vs funded project numbers). Project information was then added to the website and student application form for students to apply directly to funded projects. Student applications closed March 21st, 2022. We received 101 student applications (see Table 2). Along with contact details, students were required to give a student statement as to why they wanted to be considered for this program/project and uploaded a current, anonymized CV. Students were deemed eligible if they were a current UBC student in Year 2+ for non-MD students and in Year 1 for MD students. Students were also asked to self-identify as an Indigenous student or a student with a disability to be automatically entered to receive the Faculty of Medicine Multidisciplinary Research Award for Excellence. Project supervisors were given an anonymized list of eligible students (and their student statements and CVs) to interview. Supervisors rank ordered their top five students non-MD students and top 3 MD students from the list and were assigned 2 non-MD students and 1 MD student (optional) based on all other rankings with 36 students being funded. Students were notified in mid-April, 2022 and started the program on May 1st, 2022.

Criterion	Points	Notes
Project Summary The project must be based on a clear and testable research question(s) or hypothesis. Projects not meeting this requirement are not eligible for the FoM MRPM.	**60 points**	This section should address the scientific merit and feasibility of the proposed project. Considerations when scoring this section include:
		• Clear interdisciplinary/multidisciplinary focus
		• Clear rationale for the proposed research approach and methodology, including the context within the relevant field of research.
		• Clear and testable research question or hypothesis.
		• Feasibility of the research approach including the project timeline.
		• Expected project outcomes.
Benefit to the Student Students should benefit from their involvement and come	**40 points**	This section must address how involvement in this project will help the student gain an understanding of how high-quality research is conducted. This includes addressing the opportunities to learn new skills (or develop existing skills) in the context of the following learning objectives (**as applicable – not all will be applicable to all projects**). As a result of their FoM MRPM experience the student will gain an understanding of:

away with new knowledge, new skills, and a better understanding of what interdisciplinary/multidisciplinary research entails.		• How to generate testable research questions and/or hypotheses
		• How to critically evaluate & analyze existing literature/data
		• The principles of experimental design
		• The ethical principles of research
		• How to critically analyze data; appropriate statistical analyses
		• Effective scientific communication (such as presentations, manuscripts, guidelines, patient learning materials, etc.)
		• Specific techniques/skills required for the project (of lesser importance in scoring than the above learning objectives)
		Additional considerations when scoring this section:
		• The student's learning objectives and role are clearly defined.
		• The fulfillment of additional learning objectives (not discussed above) related to the conduct of medical research.
		• Student has the opportunity to interact with and learn from other researchers (will help the student gain a broader understanding of what research entails).
		• The project has strong research and educational merit.
		• The project can be completed in the time available.

Table 1. Adjudicator scoresheet.

	Applications	Funded
Supervisor	**16**	**16**
Student	**101**	**36**

Table 2. Total number of project and student applications and funded awardees for the 2022 MRPM Pilot Project Research Projects

Figure 1. Disciplines involved in the 2022 FoM MRPM

Supervisors

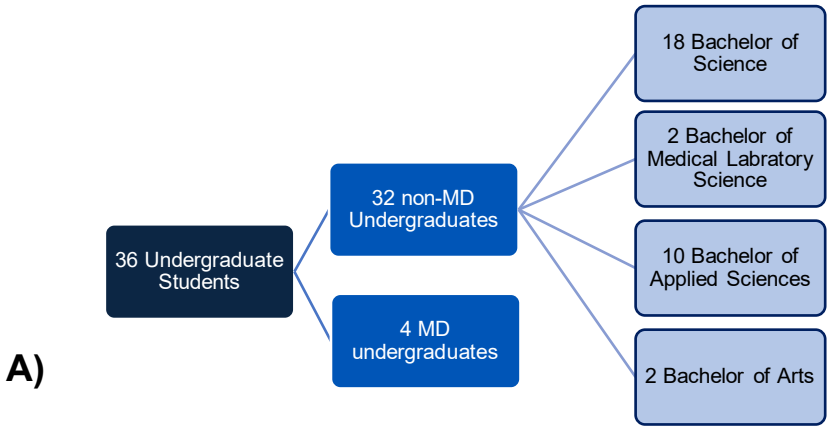
16 FoM supervisors and 16 non-FoM co-supervisors were a part of the 2022 FoM MRPM. Primary supervisors were required to hold a FoM appointment. Co-supervisors were required to hold appointments outside of the FoM. There were no restrictions on the co-supervisor's Faculty or Department except that they could not be primarily appointed by the FoM. The only exception was that co-supervisors could be appointed through the School of Biomedical Engineering. This was to encourage collaborations across faculties and departments and facilitate multidisciplinary/interdisciplinary research. These co-supervisors were from the School of Kinesiology, Department of Microbiology and Immunology, Department of Electrical and Computer Engineering, etc. (see Figure 1 for full list of co-supervisor disciplines).

Undergraduate Students

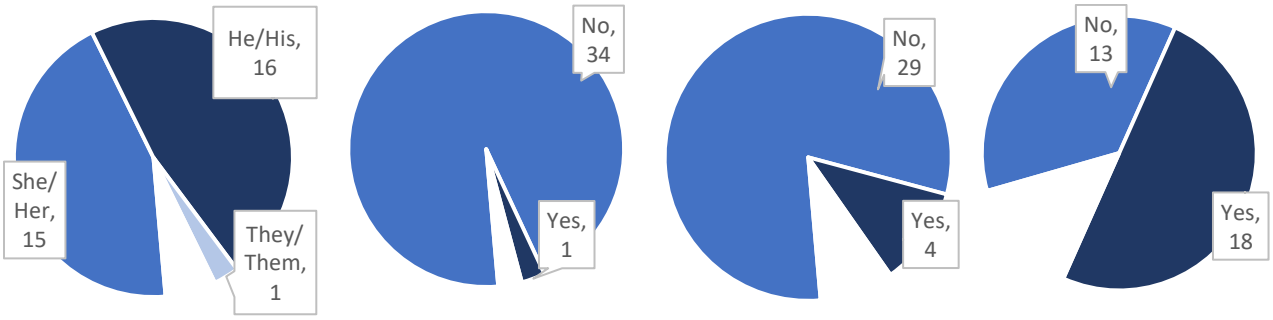
A total of 36 students were appointed to the FoM MRPM program for summer 2022. Two upper year non-MD undergraduates (years 2+ of their program) were assigned to each of the 16 funded research projects and one first-year MD student was assigned to four research projects (based on supervisor interest; see Figure 2A for program breakdown). We also asked additional self-identifying demographic information to better understand our student awardees. Of the 36 student awardees, 15 identified as she/her, 16 identified as he/him, 1 identified as they/them, and 2 declined to answer (Figure 2B). Additionally, one student self-identified as Indigenous (Figure 2C), 4 self-identified as a person with a disability (Figure 2D), and 18 self-identified as a visible minority in Canada (Figure 2E).

"I have seen the students become increasingly independent, take ownership of their work, and become more confident in the findings they present. This program allowed the students to develop their research skills full-time over the summer, where they devoted their time becoming proficient in skills essential for high-quality research."

-MRPM Supervisor



A)



B) Student Preferred Pronoun

C) *"Do you identify as Indigenous, that is, First Nation (North American Indian), Métis or Inuk (Inuit)?"*

D) *"Do you identify as a person with a disability as described in the Accessible Canada Act?"*

E) *"Do you identify as a member of a visible minority in Canada?"*

Figure 2. A) Number and program of student awardees. B)-E) Student demographic information

Funding

Funding was provided for research projects in the form of student stipends. Non-MD Undergraduates received at least $8,400 for 16-weeks of full-time research. Of this total, $6,000 was provided by the FoM with supervisors contributing at least $2,400. MD students received $3,200, all of which was provided by the FoM. The total funding amount for this program was ~$297 000 (see Table 3 for breakdown). Funding was derived from a combination of FoM endowments and supervisor contributions.

Total Program Funding	Total Internal Funding	Total Supervisor Contributions
$296,806.74	**$214,400.00**	**$82,406.74**

Table 3. Funding breakdown for the 2022 MRPM

Your generosity has had a huge impact on our groups ability to do conduct research that will have an impact on how patients are managed. Also, the students have had such an amazing time this summer - the scholarship really motivated them and rewarded them to do an excellent job from start to finish. Our group really got excellent value from this investment, and no doubt it will make an impact on the students' decision and ability to continue in research and/or medical sciences."

-MRPM Supervisor

Workshops

Workshop Overview

Workshop 1

The theme of this workshop was multidisciplinary research. During the first part of this workshop, students introduced themselves and their research project to the group to get to know each other and the scope of research being done for the project. We were also honored to have Dr. Stuart Turvey, a professor and Canada Research Chair in Pediatric Precision Health at UBC, give an inspiring talk on multidisciplinary research. Finally, we had all the Postgraduate Student Advisors on the project present to provide a lab experience and graduate school question and answer session to the students.

"I would like to thank the donors for helping to produce such a powerful program for young students and future researchers/clinicians. The FoM MRPM has allowed me to pursue a project in my field of interest and to work alongside a diverse selection of experts and other bright undergraduates. This experience will surely be extremely valuable to me in my academic and clinical career."

-MRPM Student

Workshop 2

The theme of the second workshop was research communication. Here, Dr. Kaylee Byers from SciCATS, gave a presentation on effective research communication to students. Nikolas Krstic from the Applied Statistics and Data Science (ASDa) group also answered questions from students. Prior to this workshop students were required to watch one of four videos on data analysis that was most relevant to their own research. They were then asked to come up with two questions to pose to Nikolas during the workshop's Q & A session. Finally, we provided information on the upcoming third workshop, the student research conference.

Workshop 3

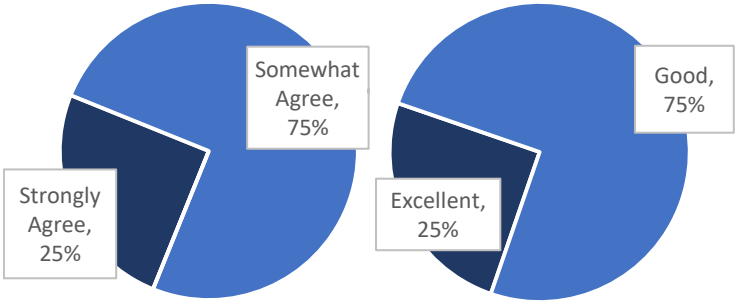
The third workshop was the student research conference. Students built a one-slide poster-like powerpoint presentation and gave a 5-minute presentation on the results of their summer research project to the group with up to 2-minutes of questions from their peers. Students evaluated each other's presentation and the highest scoring presentation won best presentation and received a certificate of award (see Appendix 1 for winning presentation).

Workshop Evaluation

To improve future workshops and evaluate the success of the current workshop series we disseminated evaluation surveys for student feedback following each workshop. Students were required to attend these three workshops and so besides one or two absent due to illness or previous plans, all students were in attendance either virtually or in-person. Students rated their experience with the individual workshops and with the workshops overall. **We had positive feedback from all three workshops, with all three workshops receiving good to excellent ratings above 88%** (see Table 4).

Workshops	Percentage of students agreeing that the topic chosen was a good topic for the workshop	Percentage of students agreeing that the overall satisfaction with the workshop was good to excellent
Workshop 1: Multidisciplinary Research & Graduate School Q & A	**91%**	**92%**
Workshop 2: Research Communication & Data Analysis Q & A	**90%**	**89%**
Workshop 3: Student Research Conference	**100%**	**100%**

Table 4. Evaluation breakdown by workshop



A) *"Including all three workshops in the summer research program was helpful or informative"*

B) *"Overall satisfaction with all three workshops was good or excellent"*

"I was hoping to get a holistic research experience and to have a lot of autonomy and responsibility. The program blew this expectation out of the water. I got to do everything on our study."

-MRPM Student

Figure 3. A)-B) Student responses to prompts shown in figure

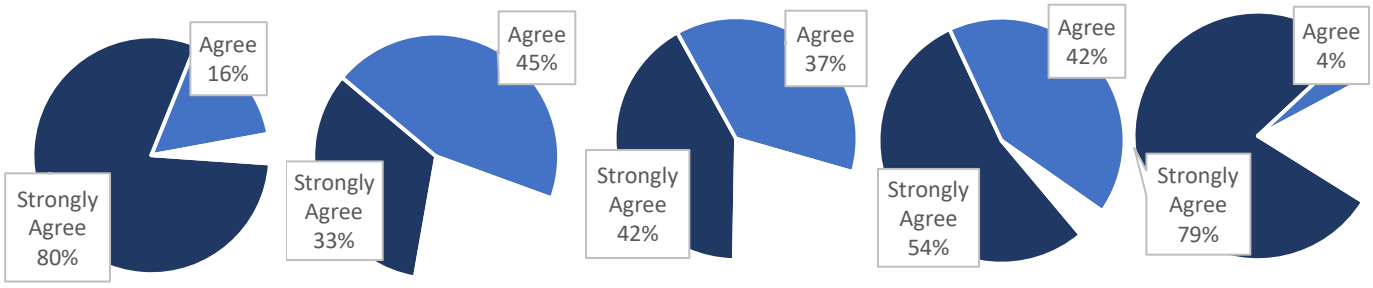
Program Evaluation

Supervisor & Postgraduate Student Advisor Feedback

Supervisors, postgraduate student advisors and undergraduate students evaluated this year's program and provided feedback for improvement. We received mostly positive feedback with 96% of supervisors reporting that this will generate future research (Figure 4A), 78% believe this has the potential to be included in a publication (Figure 4B), and 79% say this has the potential to positively impact policy, clinical practice, and/or healthcare delivery (Figure 4C). Furthermore, **96% of supervisors said this was a positive experience (Figure 4D) and 83% plan on applying in future years (Figure 4E).**

"For this project the students were critical given their expertise in computing and programming. They students were highly dedicated and focused on the aims of the project and simply put, we could not have done this without them."

-MRPM Supervisor



A) *"This study will generate further research"*

B) *"The results have the potential to be included in a publication"*

C) *"The results have the potential to positively influence policy, clinical practice and/or health care*

D) *"My overall FoM MRPM experience was*

E) *"I plan to apply to the FoM MRPM in future years"*

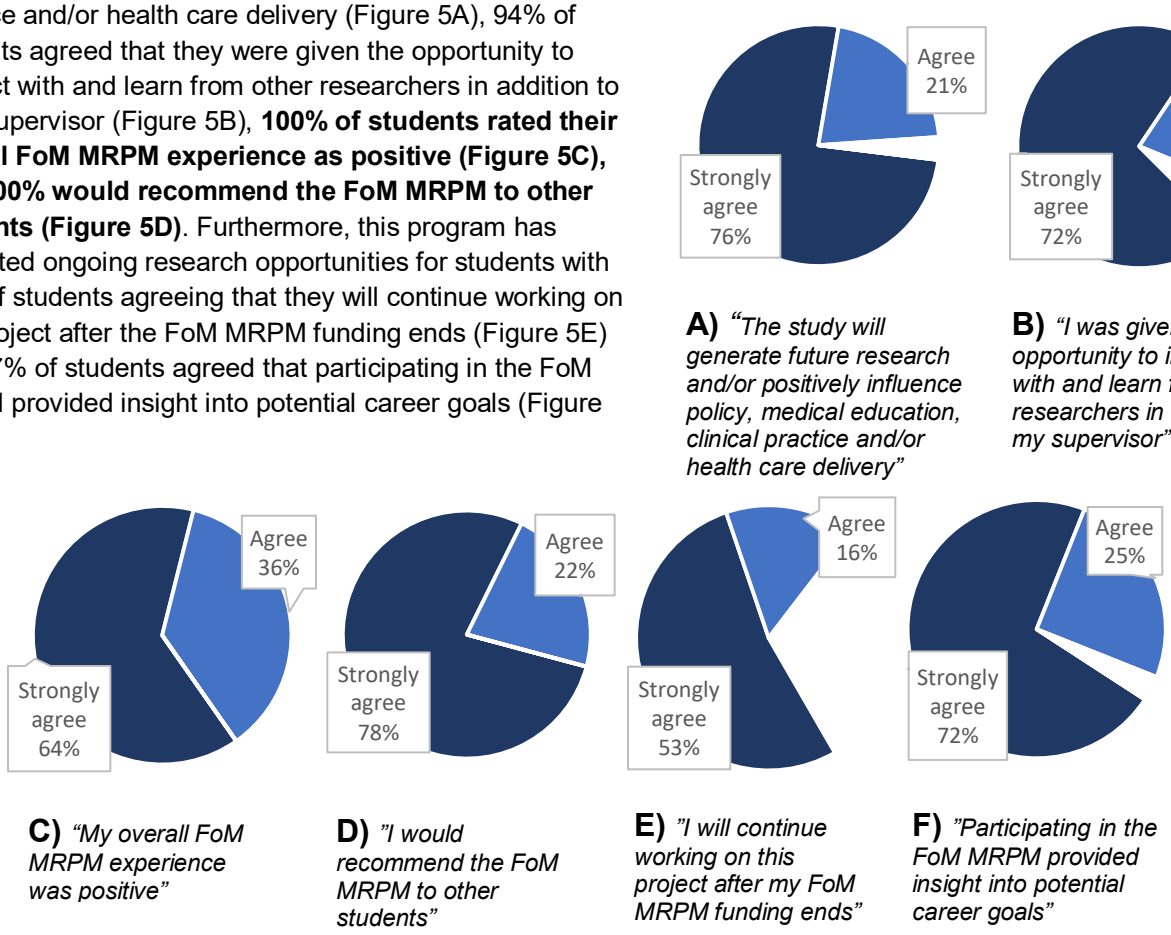
Figure 4. Supervisor and Postgraduate Student Advisor responses to the prompts in figure

"Thank you for providing this opportunity for our group to establish new research collaborations. The MRPM was a catalyst for us to explore new interdisciplinary projects."

-MRPM Supervisor

Undergraduate Student Feedback

Students also evaluated the program and provided feedback. We again received mostly positive feedback with 97% of students saying that this will generate future research and/or positively influence policy, medical education, clinical practice and/or health care delivery (Figure 5A), 94% of students agreed that they were given the opportunity to interact with and learn from other researchers in addition to their supervisor (Figure 5B), **100% of students rated their overall FoM MRPM experience as positive (Figure 5C), and 100% would recommend the FoM MRPM to other students (Figure 5D)**. Furthermore, this program has facilitated ongoing research opportunities for students with 69% of students agreeing that they will continue working on this project after the FoM MRPM funding ends (Figure 5E) and 97% of students agreed that participating in the FoM MRPM provided insight into potential career goals (Figure 5F).



A) *"The study will generate future research and/or positively influence policy, medical education, clinical practice and/or health care delivery"*

B) *"I was given the opportunity to interact with and learn from other researchers in addition to my supervisor"*

C) *"My overall FoM MRPM experience was positive"*

D) *"I would recommend the FoM MRPM to other students"*

E) *"I will continue working on this project after my FoM MRPM funding ends"*

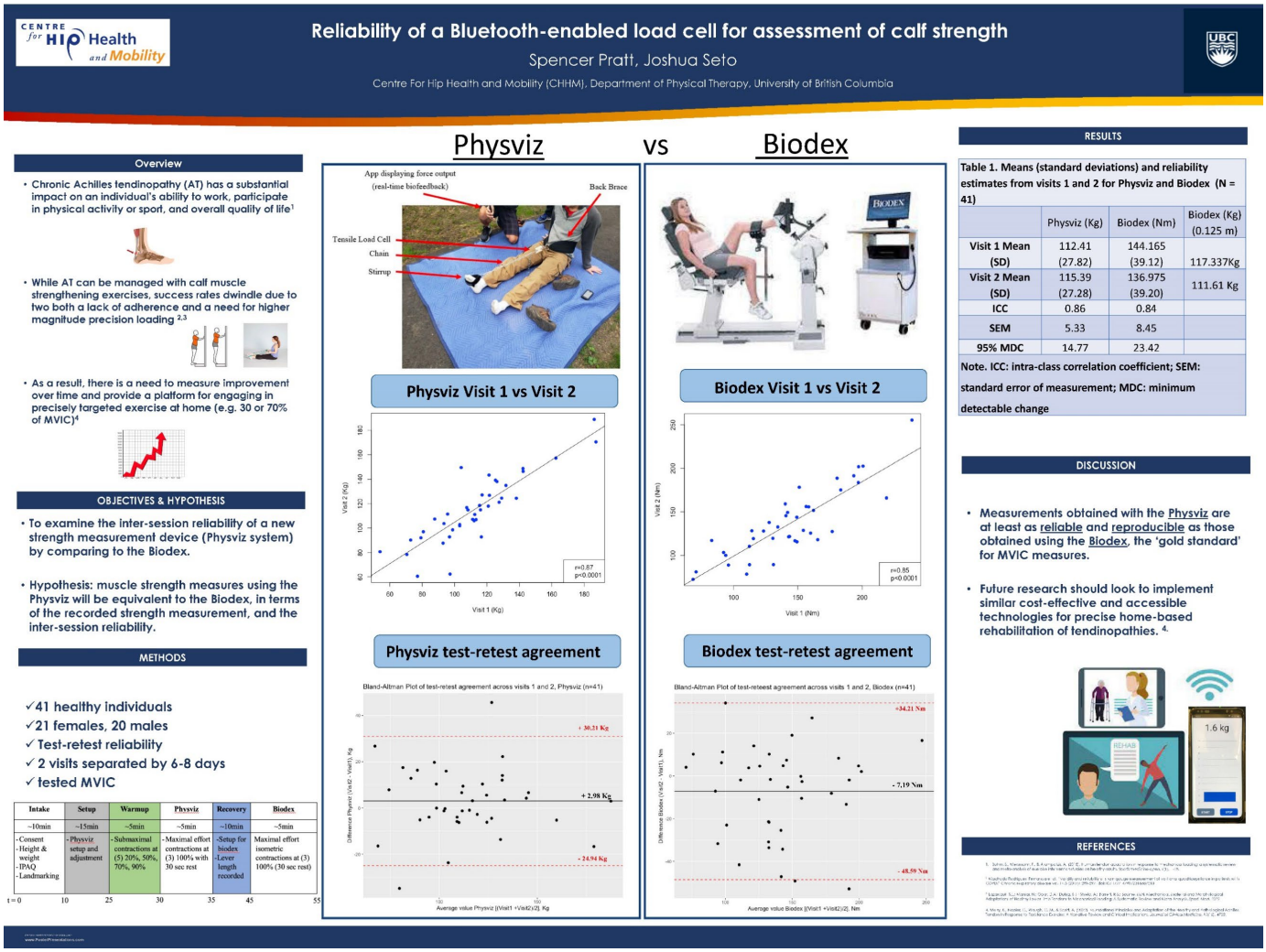
F) *"Participating in the FoM MRPM provided insight into potential career goals"*

Figure 5. Student responses to the prompts in figure

"The FoM MRPM experience by far exceeded any expectations that I may have had! I think the most amazing part of the experience was being able to participate as part of the research groups and getting to see what they were working on as well was a bonus. Having a mentor that was so knowledgeable and supportive really made all the difference and cannot thank them enough for the time they spent training me!"

-MRPM Student

Appendix 1: Example winning poster at Student Research Conference



Appendix 2: Project Summaries

Electro-transformation of Mycobacterium abscessus

What question(s) does your project aim to address?

The goal of this project is to construct M. abscessus strains that produce green fluorescent (GFP) or red fluorescent proteins (RFP) by transferring the GFP/RFP DNA into the bacterial cells. The M. abscessus strains are obtained from a patient in the clinic, so they can cause more damage to human bodies and are more difficult to treat comparing to the strains that are commonly studied in lab.

Project Overview

The clinical sample of M. abscessus formed colonies (a group of bacteria derived from one parent bacterium) with different appearances, which were roughly classified as rough colony and smooth colony. The difference in morphology could lead to different response to antibiotics. Therefore, we needed to separate smooth colonies from rough colonies first.

The method I used to introduce the foreign genome into the bacteria was called electroporation transformation. It applied electrical pulses to punch holes on bacterial membrane so that the foreign DNA can enter.

The foreign DNA also encoded a selective resistant gene which enable the bacteria to survive in the environment containing certain antibiotic, while the bacteria without the foreign were killed by the antibiotic. Hygromycin was used as my selective antibiotic.

After electroporation, the bacteria were treated with hygromycin. Bacteria without foreign DNA were also included as control.

Results/Impact

In the first attempt, it was found that the bacteria without foreign DNA survived under hygromycin treatment instead of being killed. What could have happened was that the clinical bacterial strains could have already resistant to hygromycin. Thus, hygromycin can no longer be used as selective antibiotic. It will be replaced by kanamycin in the second attempt.

The reason we want the bacteria to produce fluorescent proteins is that it allows us to measure how many bacteria died after a treatment and thus help us to determine the effectiveness of a drug or therapy. It is faster and more sensitive than the traditional UV-vis spectrophotometry.

Understanding breakthrough neuropathic pain

What question(s) does your project aim to address?

The aim of these projects was firstly, to synthesize data on the prevalence and distinct features of non-malignant BTP. Secondly, we aimed to characterize the BTP experiences of non-cancer patients longitudinally over a 3-month period through daily reports in a smartphone application. The experiences we aimed to capture through the smartphone application included factors such as the types of pain sensations experienced, the relationship between baseline pain and BTP, and the impact of BTP on quality of life.

Project Overview

Our project comprises two phases. One of them is a systematic review which will synthesize all information on breakthrough pain in non-cancer chronic pain patients. Our goal is to characterize multiple characteristics of breakthrough pain including intensity, duration, breakthrough medication, and frequency.

Additionally, this project includes an ecological study, which assesses patients' experiences of pain in real-time through a smartphone application. For this component of the project, chronic pain participants provide daily BTP and weekly baseline pain reports over 90 days. These reports characterize the intensity and sensations of both baseline and BTP, as well as other factors (i.e., what may have triggered the BTP, etc). Using this method of real-time sampling is beneficial in that it can capture trends over time, has high ecological validity, and avoids issues with recall (Todd et al., 2019).

Results/Impact

In our comprehensive literature search, we found a substantial knowledge gap surrounding the characteristics of noncancer BTP. From our preliminary findings, we discovered that BTP prevalence in noncancer patients was often comparable and at times higher than the prevalence in the cancer population. This highlights the urgency of further investigating BTP in noncancer pain conditions. The difficulty in treating BTP may be attributed to the high variability in the frequency, duration and intensity of episodes. The rapid exacerbation of pain renders it challenging to treat effectively with most pharmacological interventions. So far, short-acting opioids have been a frequent addition to the drug regimen of BTP individuals. Yet, given that most patients are chronic opioid users, additional BTP drugs can be detrimental to long-term health, and importantly, several studies show that the pain-reducing effect is frequently insufficient in masking BTP. To create interventions that are effective and suitable, it is imperative to develop a foundational understanding of the characteristics of BTP. We are still in the process of working on this portion of the project and look forward to bringing to light the need for additional BTP research in the noncancer population.

The ecological component of the project (i.e., the longitudinal data being collected through the smartphone application) is currently ongoing. At present, data is being actively collected from six participants, with more participants being added to enrollment over time. We anticipate that collectively, by the end of the study we will have rich and detailed information that captures the sensations of baseline pain and BTP, as well as trends that occur over time. Ultimately, our work suggests there is a lack of information on non-cancer BTP, and that approaches for non-cancer BTP management may be drawn from strategies used in cancer populations, which may not be ideal for non-cancer patients.
We hope that by characterizing patients' lived experiences with pain we can gain insight into numerous factors, including the longitudinal relationship between baseline and BTP, as well as aspects of the burden of BTP on patients' lives and the healthcare system (i.e., ER visits due to pain). This research may raise awareness of the issues surrounding non-cancer BTP, and help pave the way for improved BTP management in non-cancer patients.

Capture of human movement in the real world: Integration of markerless motion capture with gamified rehabilitation

What question(s) does your project aim to address?

For this project, our aim is to validate whether we can use DeepLabCut to capture complex human kinematic data in 2D and 3D for future use in rehabilitation tasks. Thus, we can
1. Obtain 2D position data using DeepLabCut within an error rate of 5 pixels.
2. Create 2D kinematic plots and 3D positioning graphs using the position data.

Project Overview

Our project started off with 2D video training in DeepLabCut. We first extracted our desired frames and manually labeled them with the body parts we want, and allowed the network to learn and train for hundreds of thousands iterations, using the given position data. We then used the model to analyze novel videos and the trained network would output the results, including the body part coordinates for every frame. Using the analysis results, we utilized the DLC2Kinematics functions as tools to extract joint velocity and angles. In addition, once we obtained the 2D training data for 2 cameras, we triangulated the results using the calibration data of both cameras, and acquired 3D data and graphs using external software such as Python and Matlab.

Both Anna and Kaylee worked on acquiring video data to analyze on healthy and stoke participants of a variety of tasks related to rehabilitation. Both students also had hands on experience using the DeepLabCut package and related Python commands for analyzing data in 2D and 3D. Finally, both students worked on establishing a feasible processing pipeline for this project as well as conducting related literature reviews.

Results/Impact

Overall, we were able to use DeepLabCut for analyzing video data of subjects for gamified rehabilitation purposes. The key benefits of the components of our project is that we use a cost-effective, less cumbersome system that can be used in many diverse environments and has the flexibility of changing points of interest during the post-processing stage. These are particularly beneficial since the current steps for the project is acquiring real data on stroke participants towards rehabilitation tasks in real times. There is a direct benefit of its functionality and versatility so that we can better understand rehabilitation in real world environments such as a stroke patient's home. This will be aimed towards establishing as full system involving a Kinect rehabilitation game for stroke patients to use at their homes as they see fit. Video and related data can then be used to evaluate and broaden our understanding of the patient's rehabilitation progress by a trained physiotherapist/researcher.

Project discovery: COVID-19

What question(s) does your project aim to address?

The research project hypothesizes that the consensus generated from combining many citizen science results demarking clusters of flow cytometry data will inform a machine learning algorithm that can produce a more accurate and meaningful result for the research community.

Project Overview

The project used publicly available flow cytometry data to generate a machine learning (ML) algorithm that could accurately identify cell clusters. It did this through taking homogeneous datasets and increasing the heterogeneity (with student 2 assisting in this regard) before sending them to EVE online, a massively multiplayer online game to generate millions of datasets using citizen scientists. These datasets were used to train the ML algorithm for producing a more accurate and meaningful result for the research community. The efficacy of the ML algorithm was evaluated through a "sanity check" designed by student 1.

In the project, student 1 mainly focused on producing an unsupervised algorithm that outputs the cluster number of the bivariate plots based on density information. The main concept is to divide the plots into sections based on the variety of features on density curves and analyze each section individually. The features indicated the size, position and density of the supposed cell populations. Within each section, the same analysis will be conducted and the number of specific features will be counted as clusters. Hence, the sum of cluster numbers is the total cluster number of the bivariate plot. This entire approach will be conducted on both the x and the y axis and the final cluster number will be output after evaluating both cluster numbers that come from each axis.

Student 2 focused on reducing the plot homogeneity before sending the flow cytometry datasets to EVE Online. This was done through a program called FlowSim that used a technique known as near duplicate detection, where the density of each plot was compared in a pairwise fashion. If the two were similar, they would be grouped using a community algorithm, and a random number of the homogeneous plots deleted. This could be iterated a number of times, with a higher number of cycles of the program producing data of higher heterogeneity. The student primarily worked on streamlining FlowSim execution via a resource management system called SLURM, executing this on all datasets that needed to be sent to FlowSim. They also assisted in optimizing and testing FlowSim's functionality with hundreds of thousands of flow cytometry plots.

Results/Impact

In the project, the cluster-number algorithm has an accuracy of 53% and 97% of the testing data has a result that is only 1 cluster different from the true values. Although the accuracy is less than ideal currently, it did demonstrate significant and obtainable potential to accurately predict the cluster number. This is one of the first steps to combining the many flow cytometry bivariate plots. Without the predicted cluster number, the ML algorithm that combines the many plots cannot be carried out. Hence, it is essential to output an accurate cluster number.

FlowSim was used to increase heterogeneity before feeding flow cytometry to citizen scientists in EVE Online. The filtering of these plots was found to be effective, and highly accurate when compared to manual consensus results generated by the team, reflecting them almost perfectly.

Overall, the project is very impactful, potentially streamlining flow cytometry analysis for scientists globally by automating post-processing and identifying possible cell populations of interest. This has the potential to lead to groundbreaking vaccine, therapeutic, and immunology-based developments in all areas of biological science.

Analytical validation of silicon photonic biosensors

What question(s) does your project aim to address?

My goal is to build a high-resolution, inexpensive device to functionalize the biosensors; the device must not scratch the silicon chip surface, allowing for high-speed fluid switching and printing.

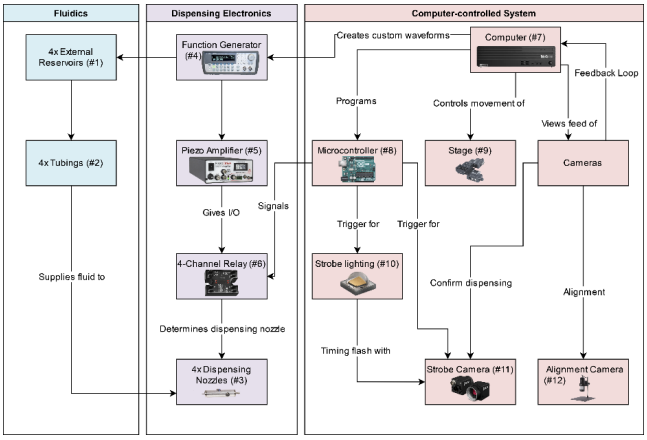
Project Overview

As described above, one way to functionalize tens of small-sized sensors (~0.1 mm) all on the same chip with different chemistries, otherwise known as multiplexing, is through inkjet printing. To create an in-house printer, a literature review is needed to familiarize with existing commercial designs, followed by listing essential components that would form the building blocks of the design. Each part would then be benchmarked using weighted evaluation criteria derived from the literature, and the highest ranked options would be purchased from suppliers and will be assembled together, integrating with a software design for the device to operate.

My role was to present a printer design optimized for biosensor functionalization that dispenses four separate “inks” through four nozzles to rapidly functionalize multiplexed sensors on silicon photonic chips. It also included the literature, benchmarking, design, documentation, and purchase of electronic and mechanical components.

Results/Impact

The proposed printer system design (attached below) provides an overview of the direct result of my project towards analytical validation of multiplexed silicon photonic biosensors. Although the printer was not completed within the timeframe, most of the components have been benchmarked, purchased, and code for software components of the design has been partially written and well documented.



Since the completed printer will be able to do simultaneous sensing, it will drastically reduce the time of experimentation from a manual process of individual functionalization to a process that can automate the dispensing process quickly and efficiently. These experiments on silicon photonic chips are crucial due to its potential in medical diagnostics. Indeed, the field of biosensors improves on deficiencies caused by the need to evaluate conditions within centralized lab locations rather than direct-to-consumer products. This can cause problems especially in rural regions where transportation is difficult and lengthy travel times alter the sample initially obtained from the patient. With silicon photonics, compact designs coupled with low cost allow for easy access by the general public once the technology is more mature. This project works towards that goal of future commercialization of silicon photonic biosensors as an alternative to traditional medical diagnostics.

Model for injury reduction in anterior cruciate ligament (MIRACL)

What question(s) does your project aim to address?

Aim(s): to develop an effective and clinically proven three-part ACL injury reduction program.
Does our MIRACL injury prevention program reduce the number of injuries that occurred over a season?
Using the L.E.S.S. (Landing Error Scoring System) criteria, do the individuals reduce their error score?
Does the PEP exercise program reduce injuries in skiing?

Project Overview

METHODOLOGY
An estimated 200-400 employees that ski will be recruited from Big White Ski Resort. Specifically, ski patrollers, and instructors will be recruited however everyone is invited to complete the program. They complete an intake form and the consent form prior to the start of the program outlining any health-related issues. As part of their standard pre-season preparation which starts in early November, employees come to Big White to do training and preparation.

1. Registered participants will complete the ten-second vertical drop test and be filmed. (Both the frontal and sagittal view.) The films will be evaluated offsite using the L.E.S.S criteria to determine high-risk and low risk groups.
2. Participants will watch a situational awareness video teaching participants about knee anatomy, the risks involved, the mechanisms of injury and how to prevent them. This short video will be watched once at the start of the pre-season. Then, it will be watched once a month by the employees during the ski season
3. Participants will then complete the PEP program 15-20 minutes daily for five days week. This will be completed over the course of three-week pre-season preparation.
4. At the end of the preseason, participants will be measured again to identify if any changes in risk had occurred through the use of the PEP.
5. Finally, LESS evaluation will occur for a third time at the end of the ski season to see whether the training was retained by the employee.
6. Any injuries that occurred at the workplace will be recorded and confirmed through medical records and through WorkSafe BC.

TASKS
The first phase of the project was completed over the summer of 2022. This included in designing a methodology based on prior research, consulting clinical ethicists, former Olympic athletes, and members of the affected Big White community. The next phase of this project will begin in the fall/winter of 2022. This includes actually gathering completed forms and collecting data.
Anthony and Rahma were both responsible for the design and implementation of the program. Anthony developed the research website and was responsible for conducting literature reviews, modeling the mechanisms of injury and designing an original program based upon prior research. Rahma was responsible for design and implementation: consulting with clinical ethics board, creating medical consent forms and contacting outside advisors.

Results/Impact

The results of our investigation can inform workplace safety and training that takes place at ski resorts. If our results are promising in terms of injury reduction, this can lead to the implementation of our program across ski resorts in British Columbia preventing hundreds of unnecessary knee injuries. This will reduce costs for worker compensation and reduce unnecessary surgeries clogging up our in-patient healthcare facilities.

Impacts/Potential users of our research:

• Ski Resorts Owners & Big White Chamber of Commerce - it would be in the ski resort owners and management best interest to reduce insurance premiums, reduce costs in worker's compensation and hiring temporary employees. Cheap and effective way to reduce business costs.
• Employees at Ski Resort – To prevent anterior cruciate ligament injuries and other serious skiing injuries
• WorkSafe BC – WorkSafe it would be in their interest as it is one of the government mandates for this organization: to reduce injuries at the workplace. A cheap and cost-effective exercise program would accomplish one of their priorities.
• Athletic Associations & Highschool Gym Teachers/Coaches – Youth sport associations and coaches could potentially benefit from the findings of our study a use to implement it in their warm-up and training sessions.

Development and application of natural language processing and machine learning to accelerate breast cancer research

What question(s) does your project aim to address?

We hypothesize that a transformer model with NLP will be more accurate than a rule-based algorithm and have either a higher or equivalent accuracy to manual extraction by reviewers.

Project Overview

Over 2,000 synoptic (or structured) and 300 non-synoptic (or non-structured) breast cancer pathologic reports were annotated by both Annah and Christy for testing and validating the transformer model. The reports were pulled from Providence Health Services Authority and involved patients who were diagnosed with either ductal carcinoma in situ, an invasive carcinoma, or both.

In order to efficiently annotate reports, Annah and Christy had to read many research papers and medical seminars to fully understand the terminology that is used by the medical professionals that write the reports. They worked with another co-op student in the lab and a team of data scientists to establish effective strategies for annotating reports, which they turned into an SOP (standard operating procedure). This was done so that the data collected from different annotators would have little to no variation and to feed the most useful information into the BERT model.

After the annotations were completed, they were able to see how the NLP and the BERT model worked and also took part in troubleshooting errors to improve the accuracy of the model.

To improve their understanding of NLP, machine learning and patient care, they both conducted separate scoping reviews to better grasp how machine learning and natural language processing can be applied to accelerate breast cancer research. Annah's paper, "Applications of Natural Language Processing in Breast Cancer Research", and Christy's paper, "Current Applications of Machine Learning in Breast Cancer Prognosis and Prediction", also explore various ways that machine learning and natural language processing can be used.

At the end of the summer, both Annah and Christy also had the opportunity to work on one other project, VascuLens, which is an augmented reality projector that projects personalized vasculature onto each patient. They learned how to fill in and submit RIse applications, write consent letters and create info sheets related to the procedure.

Results/Impact

Our synoptic reports had a 97.8% and 98.6% accuracy on fields of interests that were and were not present in the pathological reports, respectively. It can take an experienced reviewer weeks to annotate hundreds of reports, but the model is able to complete thousands within a day or two. The data is then summarized for further research.
Our findings are promising, and we hope to further develop the model to extract data and information from all types of cancer pathology reports. The system, which we have preemptively named OncoAid, can then be implemented throughout the province. This will improve cancer research as a whole, so that researchers not only have a large amount of data to work with, but also real-time data.

Impact of acute stress on experimental pain: A systematic review

What question(s) does your project aim to address?

To explore this discrepancy: does the type of acute experimental stressor influence an analgesic vs hyperalgesic response? To address this overarching question, we conducted a systematic review to 1) determine if the type of experimental stress (e.g., Trier Social Stress Test, Stroop test, etc) significantly effects pain ratings and 2) explore if the method of pain assessment is a predictive factor (covariate) in the stress-pain relationship.

Project Overview

The search was guided by the design strategy Problem, Intervention, Control and Outcome (PICO) question: In studies involving experimental acute stress and an experimental pain measure, does the type of experimental stress (e.g., Trier social stress test, Stroop test, etc.) effect pain outcomes (e.g., pressure pain threshold, mechanical pinprick sensitivity, heat pain threshold, flare size, etc.) in healthy populations? Five databases were searched: MEDLINE, EMBASE; CINAHL; PsycInfo; Cochrane Database of Systematic Reviews. Several strategies were implemented to search grey literature.

This process yielded a total of 18168 studies. These studies were then reviewed independently by two reviewers (Jaimie Lee and Nazanin Sadoughian) based on our set of inclusion and exclusion criteria. Studies were included if they contained an experimental stress task that was quantified by either an objective measure (heart rate, blood pressure, cardiac output) or a subjective measure (self-reported level of stress), as well as an experimental pain outcome. With this criteria, 53 studies were included in review.

Results/Impact

Analgesia was observed more often than hyperalgesia in response to experimental stress; which agrees with the theory that stress duration plays a role in pain responses; but the results do not show a clear relationship. Moreover, many studies showed no effect of acute stress on pain. This observation suggests the presence of confounding variables (such as sleep duration/quality or diet); but it also implies an influence of the type of experimental stress and method of pain assessment on pain responses. These relationships can have substantial clinical applications for chronic pain populations and guide future research investigating the paradoxical relationship between stress and pain. The narrow scope of study populations without chronic pain is an essential first step in determining the relationship between stress and pain without the numerous confounding variables that the complex condition of chronic pain presents (e.g., baseline medication use, sleep deprivation, lack of social connection, reduced movement, pain catastrophizing, long-term central sensitization). Ultimately, the end goal of this review is to assess the direction of these relationships through further analysis of data.

Quantitative localization of autonomic neurons activated by exercise and neuromodulation after spinal cord injury

What question(s) does your project aim to address?

We hypothesize that transcutaneous electrical spinal cord stimulation diminishes the cardiovascular abnormalities that occur due to AD by activating large-diameter afferents and inhibitory interneurons. The spinal cord can be made transparent via the tissue clearing method called CUBIC and identified neurons activated by TSCS immunohistochemistry through C-fos staining.

Project Overview

Research process

Transcutaneous electrical stimulation

1. All rats were stimulated with TSCS. Self-adhesive mini-electrodes were placed on the back to noninvasively stimulate the spinal cord through the skin at 30hz.

Research timeline

2. One day 1 of the experiment, all rats received a transection (complete cut of the spinal cord) at the third thoracic segment. Then, the rats were divided into 2 groups.
3. Group 1 (Tx): Received Cardiovascular assessments and colorectal distention (CRD). CRD is a method of reliably triggering AD in rodents. A balloon-tipped catheter was inserted into the rectum and inflated. Inflation causes CRD, which stimulates the rectum leading to AD. Cardiovascular Assessments were conducted by recording beat by beat BP using a wireless pressure transducer implant, allowing us to quantify the severity of AD through the difference in BP measurements, obtained during CRD and at rest.
4. Group 2 (Tx with TSCS): received CA , CRD, same as group 1 but they also received TSCS.
5. CUBIC: Following euthanasia and tissue dissection spinal cords were made transparent using CUBIC, a method of tissue clearing. CUBIC extracts lipids and matches the refractive indices in the tissue, rendering it visually transparent and allowing us to image it in 3D.
6. C-fos staining: Cleared spinal cords were immunostained for c-Fos, an immediate early gene used as a marker for activated neurons and a powerful tool to identify the number and location of activated neurons

Results/Impact

- TSCS significantly lowered AD severity, and although we were not able to completely eliminate AD, we reduced the potential for adverse cardiovascular outcomes.
- CUBIC tissue clearing methodology was successful, as spinal cord segments were made transparent.
- C-fos staining was successful as we were able to image the TSCS activated neurons.

Summary of results

TSCS promotes cardiovascular recovery after SCI. CUBIC protocol standardization was successful.

Future directions

Our Goal for future experiments is standardizing C-fos staining and quantifying the neuronal activation patterns in 3D to further explore the mechanism of TSCS on AD.

Characterization of the neurodegenerative features in the retina associated with eye and brain diseases

What question(s) does your project aim to address?

Research question 1: If the retina is a part of central nervous system, should cellular (ex: astrocytes, microglia) and molecular (ex: amyloid beta deposition) level changes that occur in the cerebral cortex and the retina be similar at young and old ages?
To answer this question, transgenic AD mice brain and eye sections at young and old ages were studied with molecular and cellular markers.

Research question 2: If the oxidative stress and inflammation crucial in the pathogenesis of AMD, could it be related with reduced antioxidant transporters in the retinal pigment epithelium (RPE) and in the choroid?
To answer this question, transgenic AMD and wild type control mice eye sections were studied with markers for angiogenesis and antioxidant transporter.

Project Overview

For the AD animal model, transgenic (Tg) mice and its non-carrier siblings (NTg) at 2 different ages: 12-16 weeks (young) and 36-40 weeks (old) were included. A total of 16 female mice were used for this study, 4 mice per group. 6 µm thick brain midsagittal sections, focused mainly on cerebral cortex, and eye cross sections, focused mainly on retina were used to determine the target proteins' expressions using double immunofluorescence staining technique. Primary antibodies 6E10, a marker for Aβ; glial fibrillary acidic protein (GFAP), a marker for astrocytes; and ionized calcium-binding adapter molecule 1 (IBA1), a marker for microglia/macrophage-specific calcium-binding protein was used.

For the AMD animal model, apolipoprotein E knockout (ApoE-KO) mice with a high fat diet and regular diet, and wild type (WT) mice at the age of 36-40 weeks (old) were included. A total of 15 female mice were used for this study, 5 mice per group. 6 µm thick eye cross sections, focused mainly on RPE and choroid regions were used to determine the target proteins' expressions using a single immunofluorescence staining technique. Primary antibodies organic cation transporter novel-type 1 (OCTN1) (rabbit polyclonal), a marker for dietary antioxidant (Ergothioneine) transporter and vascular endothelial growth factor A (VEGFA) (rabbit polyclonal) , a crucial regulator of angiogenesis were used.

All fluorescent images were captured using Zeiss LSM 800 confocal microscope with ZEN 2.6 software and the tiff images were used to calculate pixel counts using ImageJ software. Statistical Package for the Social Sciences (SPSS vs. 25) was used for the statistical analysis, and the GraphPad Prism 9 was used to generate graphs.

Results/Impact

AD: In the brain, 6E10 positive typical senile or cored Aβ plaques were found only in the old trangenic mice whereas, 6E10 expression was similar in both trangenic and non-transgenic mice and no typical plaques were identifed at young ages. Similarly, between young transgenic and non-transgenic mice, GFAP and IBA1 expressions were not significantly different in the cerebral cortex, whereas GFAP expression was significantly increased and IBA1 expression was significantly reduced in the old transgenic mice when compared with matched non-transgenic mice.

When we compared this data to the images that were captured in the eye cross sections, we found similar results. The patterns of GFAP and IBA1 were visibly consistent between the eye and brain experiments, with higher expression of GFAP and lower expression of IBA1 in the old transgenic mice. This suggests that the cellular and subcellular changes occurring in AD mouse model brain tissue are like the changes occurring in their eye tissue.

While this does seem to support our hypothesis, we have not yet completed the data analysis of the eye tissue to confirm that its changes are as significant as they are in the brain. Moving forward, we will complete this analysis and continue to examine novel biomarkers to determine which factors may be targets for treatments and therapeutic tools.

AMD: The expression level of the angiogenesis factor VEGFA in the choroid region is similar in the WT and ApoE-KO mice, whereas the expression level of the antioxidant transporter OCTN1 is stronger in the WT mice compared to the ApoE-KO mice in both RPE and choroid regions. Therefore, we conclude that the stronger expression of antioxidant transporter OCTN1 has a protective effect against oxidative stress and inflammation caused by angiogenesis in the WT mice, whereas lack of OCTN1 expression in the ApoE-KO

mice leading to increased oxidative stress and inflammation resulted with AMD. This finding emphasizes the importance of antioxidant uptake or supplementation against oxidative stress and inflammation related damages in the patients with AMD and AD.

Evaluating the role of transcervical 3D ultrasound imaging of the oropharynx during transoral robotic surgery

What question(s) does your project aim to address?

How can we validate 3D US usage in the oropharynx and integrate it into the robotic surgical system design to support our hypothesis that it will help improve patient outcomes?

Project Overview

In this project, we work with 2 main instruments: a surgical robot called Da Vinci, and an ultrasound machine that is commonly used in exam rooms. The Da Vinci robots include two parts: one is the patient-side robot that is actually doing the operation, and one is the surgeon-side console where the surgeon can operate the robot and see the views from the endoscope camera. We want to make use of ultrasound during transoral surgeries with the surgical robot to provide the surgeon with more information such as the boundary of the tumour. The boundary and geometry of the surgical region is usually viewed in CT images before the surgery for the surgeon to get an idea about the amount of tissue to remove. If real-time ultrasound can be layered on top of the CT image, we can make the surgery more successful by fully removing the tumour but not healthy tissue around it.

In the first part, our goal is to put all objects in use in one single coordinate system, so that we can easily determine their relative positions and movements. This is called calibration. We utilized a few other tools such as an optical tracker and some software to help with this process. In preparation for the calibration, we worked on custom designing accessories for the ultrasound probe using Computer-Aided Design (CAD) software, and 3D printing. We attached an optical tracker tool to the ultrasound probe for the tracker to record the position and movement of the ultrasound probe while the probe is taking images of a pointy pen. The pen also has a tracker tool attached so that we can relate their position in the world to their relative position in the ultrasound image using a software. We find the corresponding pointy pen tip in ultrasound images and the tracker coordinate system and estimate their relative transformation as the transformation between the tracker coordinate and the ultrasound image coordinate.

The ultrasound images we captured are only 2 dimensional, and we need to reconstruct the 3-dimensional structure to resemble their real geometry. The 3D ultrasound image will be manually aligned with the CT image of the patient. After aligning all the instruments in the same coordinate system, we did an ultrasound test scan of the forrearm using the in front of the optical tracker to visualize the 3D reconstruction. The reconstruction has all the muscle layers lined up in a way that is consistent with the actual anatomy. This indicates the calibration is successful. A case is made for the ultrasound probe so that in the future, the robot arm grabs the ultrasound probe during surgery so the surgeons can perform the ultrasound scanning in the console directly instead of doing free-hand scanning at the patient side.

Finally, we had the chance to work on designing a testing apparatus (phantom) for validating the mapping of the ultrasound to the MRI or CT scans. These designs also used applications of CAD to try to create a gelatin replica of the human anatomy in the neck and throat regions. Our methods of calibration, reconstruction, registration and phantom creation aim to validate the described methods for the oropharynx and integrate it into the Da Vinci robotic system.

Results/Impact

In general, our calibration was mostly successful with room for some improvements. We saw an RMS error of 12.77mm. If we redo this with some fine-tuning of the US image quality and select a lot more points, the RMS would be smaller, indicating better calibration results. The results from our test scans with the 3D Ultrasound showed that more quantitative testing with more careful and slower scanning is required for better quality results. Finally, our registration showed that US and MRI had a strong correlation since the important anatomical structures were able to be overlaid in an appropriate way. The implications of this work are directly related to patient outcomes. Creating custom testing suites and apparatuses can help in the validation of visuospatial orientation. In turn, surgeons gain more confidence in surgery, leading to better cancer resection margins and reduction of complications to patients. The future steps in this study revolve around further testing starting with the fabrication of the testing phantom described previously and intraoperative testing on patients. Finally, this work would be integrated into the surgical practice as the standard of care for TORS surgery, leading to improved patient outcomes.

Wastewater-based surveillance of infectious diseases

What question(s) does your project aim to address?

Can the capture of SARS-CoV-2 through bead-based nanotechnology (Nanotrap) generate high-quality RNA extracts
for the detection of cryptic SARS-CoV-2 lineages (variants of concern) in wastewater using long-read sequencing
technology (Oxford Nanopore Technology)? It was hypothesized that bead-based nanotechnology would outperform
the current standard operating procedure at the British Columbia Centre for Disease Control (BCCDC), ultracentrifugation, producing more concentrated and higher quality RNA extracts for testing.

Project Overview

Both students worked together in the laboratory and in bioinformatics. They both were tasked to prepare the viral concentrates with different methods, preparing the DNA library for genome sequencing (decoding), processing the data via bioinformatics and finally presenting the data visually using analytical software. To begin, wastewater samples were collected from Annacis Island wastewater treatment plant in Metro Vancouver and transported to BCCDC and UBC. Virus particles were then concentrated using four different methods: two nanotechnology-based methods (Nanotrap ER1/ER2) using enhancement reagents and nanoparticles to capture viruses, one benchmark method involving non-specific precipitation of nucleic acids by adding polyethylene glycol and salts (PEG), and one method as the BCCDC standard operating procedure (Amicon Ultrafiltration) using size -selective filters and ultracentrifugation (spinning). Genetic material was extracted from viral concentrates using automated techniques at BCCDC and immediately RTqPCR tested for SARS-CoV-2 to measure the extent of sample concentration for each method, with remaining extracts kept for genetic sequencing. This portion of the project was carried out by BCCDC research personnel due to equipment and scheduling restrictions. DNA libraries were prepared using two different multiplex PCR primer schemes, a shorter primer scheme (ARTI C) and a longer primer scheme (Midnight). Prepared DNA libraries were loaded onto Oxford Nanopore Technology equipment and sequenced. Sequencing data was processed and compared with the reference genome (original Wuhan SARS-CoV-2 strain) and with RT-qPCR results, providing visual representations of various sequencing qualities.

Results/Impact

It was found that PEG precipitation obtained the highest levels of viral concentration, while both Nanotrap methods and Amicon Ultrafiltration performed similarly. However, Nanotrap ER2 outperformed Nanotrap ER1 on all sample dates. Therefore, we confirm that Nanotrap concentrates viral genomes effectively for RT-qPCR detection when compared to standard operating procedures and benchmark methods. In regard to sequencing data from July 18th wastewater, all methods performed very well with the ARCTIC primer scheme, obtaining over 99% SARS-CoV-2 genomic coverage. PEG precipitation and Amicon ultrafiltration had the most consistent and highest coverage performance. This supports previous findings of their efficacy in genome sequencing.

In contrast, Nanotrap methods produced greater variation and slightly lower results (<1% difference), which is still quite promising. All Midnight DNA libraries yielded lower results compared to ARTIC but still obtained above 87% genomic coverage, higher than the threshold for clinic samples at BCCDC of 85%. Overall, coverage data shows that Nanotrap methods were able to produce competitive RNA extract quality to standard operating procedures that could be optimized in future trials.
Surprisingly, Nanotrap methods did not increase mapping efficiencies (percentage of DNA reads mapped/total reads) compared to PEG or Amicon despite their advertised viral specificity, showing a lower reduction of background noise in the data. We can therefore conclude that Amicon and PEG precipitation are better suited in this regard, contrary to hypothesis.

Due to lengthy standard operating protocols and expensive lab equipment, ultracentrifugation and PEG methods can be prohibitory in some circumstances. Similar experimental results exhibited by Nanotrap still offer an attractive alternative, considering the ease of use and low startup costs. Further research into its application could include streamlined and automated concentration and extraction protocols, to better control for variation in results, and minimize RNA loss from manual error. Ultimately, Nanotrap methods could still be very useful in times of urgency, remote

field hospitals, or rural communities where clinical testing is not accessible, as they produce impressive RTqPCR and competitive sequencing results. For the well-equipped lab interested in the highest quality sequencing, results suggest that ultrafiltration methods still appear to be the best choice. The direct benefit of this research to future patients is a more robust infectious disease surveillance program at BCCDC, with the future ability to detect outbreaks of variants of concern earlier than, and without the need for clinical testing.

This valuable information can be used to guide public health announcements and help district health authorities serve their constituents more effectively. Hopefully, with new technology, future outbreaks can be handled more readily and a reduction in hospitalizations and transmission can be achieved.

Validation of a bluetooth-enabled load cell for objective and accessible assessment of lower extremity strength and symmetry

What question(s) does your project aim to address?

How accurate and reliable is the novel Bluetooth-enabled Physviz system compared to the “gold standard” Biodex system for measurement of maximal calf strength?

Project Overview

41 healthy individuals (men, women, or gender diverse) were recruited. Every individual completed the same protocol, consisting of calf strength testing using the Physviz, a 10 minute break, then calf strength testing using the Biodex. Using both methods allowed for us to compare the strength measurements between each device. The participants completed the same procedure on two days separated by a week. This re-test allowed for us to determine the reliability of the devices over time.
Josh and Spencer had similar roles throughout the project, having the opportunity to carry out every step of the research process. Since COVID-19 has affected healthcare so profoundly, the students began with a literature search to better understand the advent and growth of telerehabilitation. Next, they helped to refine the prototype Physviz device by testing it on different people under different conditions. Subsequently, they built out the methods for the project by performing more pilot testing with the Physviz and Biodex and writing up a procedure.

After laying this groundwork, Spencer and Josh started recruiting healthy participants via physical posters and email. Over the next few months they brought in 41 participants to successfully complete 2 sessions in the lab. Lastly, they compiled the data and performed statistical analyses to determine the results.

After laying this groundwork, Spencer and Josh started recruiting healthy participants via physical posters and email. Over the next few months they brought in 41 participants to successfully complete 2 sessions in the lab. Lastly, they compiled the data and performed statistical analyses to determine the results.

Overall, Josh and Spencer were largely responsible for all aspects of this project and were able to learn all the skills necessary to design, carry out, and analyze a clinical research study.

Results/Impact

We were able to determine that the Physviz system is at least as reliable as the Biodex system for measuring calf strength in a seated, straight-legged position. This means that the Physviz is a viable option for objective measurement of calf strength. Furthermore, due to the nature of the Physviz device: it’s affordability, compact size, and mobile software; it provides a better solution for individuals suffering from Achilles’ tendinopathy. These patients could bring the system home and perform their exercise rehabilitation precisely and with remote clinician supervision. In the future, the Physviz, as a measurement device and as a software, could potentially be employed to improve rehabilitation of other common musculoskeletal injuries such as shoulder, elbow, or patellar tendinopathy.

Minimally invasive technologies for spinal cord injury

What question(s) does your project aim to address?

We hypothesize that optically stimulated neurons will regrow along injected scaffolds to allow linear axonal regrowth after spinal cord injuries.
This project aims to develop a system to repair an injured spinal cord by stimulating axon growth and promoting linear growth across the injury site. We hypothesize that using an optogenetic device will stimulate and
promote axon growth. As well, two methods of minimally invasive, injectable, magnetically alignable scaffolds were
proposed to guide axons across a lesion.

Project Overview

To achieve optical stimulation, Alex worked on creating a fully implantable device capable of optically stimulating the spinal cord over month-long periods. The device sits in a 3D printed biocompatible case enabling the device to remain fully implanted under the skin, with a LED probe sitting over the injury site in the spinal cord. The LED probe is flexible for precise placement underneath the vertebrae, as well as allowing the device to survive the dynamic environment of the spinal cord while causing minimal irritation. Optical stimulating specific neurons should allow regeneration and growth of axon fibers, addressing one of the issues with spinal cord injury. However, this growth will not be functional if the axons do not go across the injury site. Without proper crossing, the axons will not connect with other axons properly, and the spinal injury will be unchanged. To direct axons, we have developed and improved upon 2 methods of inserting scaffolds into a lesion
Ken worked on the first of these methods, hollow microchannels individually injected into the lesion site. Our lab has previously determined that hollow microchannels 300μm in diameter allows for axons to grow through them.

These channels are also magnetically alignable and porous, allowing nutrients to diffuse across. This project focused on optimizing the placement of these channels in the following process:

- First, these channels would be injected into a cavity 1 layer a time and then magnetically aligned
- A fixing gel would be added to secure the first layer
- We would repeat these steps to fill the cavity

By altering the length of the channels, this allows filling of a irregular 3D lesions caused by Spinal cord injury.

The second method of linear growth looked at using an injectable hydrogel in the lesion site and was done by Stephanie. The gel will guide axon growth using magnetic micro rods, sized 5 x 5 x 50 micrometres and 2.5 x 2.5 x 25 micrometres, inside the gel that is aligned along the spinal cord using magnetic fields and has a mix of medicine to prevent scar growth, aid in neuroprotection, and promote axon growth.
As this project is still in the beginning stages, the current focus is on scaffold development and optimizing the biomaterials being used. For this, we are testing the alignment properties of hydrogel using magnetic fields to characterize and optimize the biomaterials. To do this, a rat is injured to imitate a human SCI. Then at different time points after injury, a single injection of the hydrogel is administered. The animal was then perfused, and the spinal
cord was cut, stained, and imaged to look at the alignment of the micro rods. This was to help determine the best composition of the hydrogel to allow enough time for the micro rods to align before the hydrogel gelatinizes.

Results/Impact

This project is in the beginning stages of a projected six-year timeline to start trials in humans. Due to this extended timeframe, a series of smaller milestones have been made as checkpoints for the project. At the time of finishing the FoM MRPM, Stephanie had just finished a round of injuries and weas starting work on imaging the samples that came out of the trial. Due to this, there are no results of the micro rod alignment. Ultimately, the goal is to develop a treatment for SCIs. When looking at spinal cord injuries, even partial functionality can significantly improve a patient's life quality and health. Due to this, there will be a significant medical, societal, and economic impact with this project.

Using digital pathology with spatially resolved gene expression for biomarker discovery

What question(s) does your project aim to address?

1. Can tissue images discriminate Diabetic Kidney Disease (DKD) from healthy kidney tissues?
2. Can imaging data be used to predict spatial expression data?

Project Overview

Patrick

We used a dataset containing tissue samples of 3 healthy patients and 4 patients with diabetic kidney disease. We separated each sample image into multiple smaller images, called patches. After creating the patches, we split our datasets into a training set, a validation set and a test set. The training and validation sets are used in training the neural network, and the test set is used to determine the performance of the neural network. The data is placed in a neural network called AlexNet, which was previously trained on a database of images. We set the final outputs of the neural network to two, whether the sample is normal or diseased. The model was trained on the training set, and it was tuned using the validation set. After training and validation, the model was tested on a test set, where its true positive rate (rate of samples correctly identified as diseased), false positive rate (rate of samples incorrectly identified as diseased), true negative rate (rate of samples correctly identified as normal) and false negative rate (rate of samples incorrectly identified as normal). Additionally, the model's accuracy was determined by measuring the correctly predicted samples to the total number of test samples. Another indicator of the model's performance was the receiver operating curve where a higher area under the receiver operator curve shows better performance.

Gurjot

For inferring spatial gene expression, we obtained a kidney data matrix from nanostring where each column was an ROI (region of interest) image, and each row was a gene and its gene expression number for each ROI. For one gene (let's call the gene "JEAN"), we associated each ROI with its corresponding gene expression number for JEAN. We split up the datasets into a training set, a validation set and a test set. We then trained the CNN (convolutional neural network mentioned in Patrick's methods) on the training set images and their corresponding gene expression number. The model was tuned using the validation set. The model was then evaluated using the test set. With the test set, the CNN would be given an image, and the CNN would predict the gene expression number for JEAN for that image. That gene expression number would then be compared with the actual gene expression number for that image. We did this for all images in the test set. From that, we got a correlation number for predicted vs actual gene expression, to see how well the CNN could predict the gene expression for JEAN. A high positive correlation, like 0.8, would mean the CNN could well predict the gene expression for JEAN for an image. A negative correlation would mean the CNN would be bad at predicting the gene expression for JEAN for an image. We found the correlation numbers for 673 genes and ranked them in ascending order. The 673 genes are from the human organ transplant panel from Nanostring.

Results/Impact

Patrick

The GeoMx dataset predicted indicators had an accuracy very similar to the Hematoxylin & Eosin (H&E) images, and in some indicators, it outperformed the H&E images. This result is significant because the H&E images have been proven to work well with neural networks.

A Convolutional Neural Network can enable pathologists to make quick and efficient diagnoses of multiple slides by running the slide images through a network. Additionally, potential indicators may be discovered from training and testing the data on a CNN.

Gurjot

CD163 was the most well predicted gene with a correlation of 0.71. There were 84 genes with a correlation greater than 0.3 for actual vs predicted gene expression.

The use of CNNs for spatial genomics can help speed up the process of measuring gene activity in tissue samples. As well, inferring spatial gene expression using CNNs can contribute to the development of drugs that target certain gene expression markers.

High-throughput cell isolation for cancer genomics using inkjet printing

What question(s) does your project aim to address?

Can the usability and the data quality control of the Isolatrix be improved?

Project Overview

Jared Chan (BASc): A graphical user interface (GUI) was developed to aid researchers in controlling the inkjet printer, as well as in the visualization of cell isolation results. The GUI was developed using Python, to allow for rapid development, easy integration with the printer controller software, and ease of maintenance. It has to be user-friendly, allow for fine control of the printer, and provide detailed reports of printing results.

The performance of the Isolatrix is contingent on the performance of a trained neural network to classify the number of cells dispensed with each droplet. Training neural networks requires a lot of accurate labeled data. To improve our neural network, a generative adversarial network (GAN) was created. A GAN is a type of machine learning model that is capable of generating a variety of realistic data. This GAN allows us to rapidly generate more training data, which will improve the Isolatrix's classifying neural network. To obtain more training data, a microscope imaging procedure was created. After dispensing cells onto microscope slides, this procedure automatically finds the locations of cells and shortens the time spent preparing training data manually.

William Rees-Jones (BSc): Developed functions in the Python coding language for the easy visualization of cell-line trial data. These functions allow researchers to quickly graph important metrics in order to assess the quality of their sequencing data. For example, one function shows how evenly different regions across the genome were sequenced, and another function shows the amount and type of contamination in the sequencing data. Issues with the quality of the data are often caused by problems with the cell-isolation technology. Thus, these graphs will help researchers identify issues with the cell-isolation technology and refine it as necessary. The graphing functions will be used as part of the quality control phase after data has been obtained from cell-line trials, and will save future researchers the time spent aggregating data and developing their own visualization functions.

Results/Impact

A variety of key developments in the Isolatrix project were made. A GUI was developed, which integrates core functionality of the instrument allowing researchers to more quickly conduct experiments and more intuitively interpret results. The GAN is able to generate images that are as realistic as the real ones. It can generate thousands of images every minute, expanding our training dataset for the Isolatrix's neural network. It will help the Isolatrix's accuracy in determining the number of cells dispensed with each droplet. The microscope imaging procedure can semi-automatically image and accurately label training data. Researchers only have to manually go through a tenth of the data, and they can be more confident in the quality of training data produced. It saves time for researchers and improves Isolatrix's accuracy further. Functions for the visualization of trial data were developed as part of the quality control workflow, which allow researchers to quickly identify problems within their trial data, thus leading to further refinement of the Isolatrix. These developments help improve the Isolatrix, which will eventually allow scientists to obtain high-quality single-cell whole-genome sequencing data faster than previously possible. Improvements in data acquisition due to the Isolatrix may help advance the understanding of the genetic diversity within individual tumours, and thus eventually inform new therapeutic approaches to improve patient outcomes.