THE UNIVERSITY OF BRITISH COLUMBIA

School of Biomedical Engineering

Faculties of Applied Science and Medicine

SBME RESEARCH DAY

OCTOBER 31, 2023

Trainee Talks

TRAINEE TALK #1

Fereshteh Yousefirizi

Postdoc, SBME
Supervisor: Arman Rahmim

Trainee Talk Details:

Location: LSC 1001
Time: 9:45am

TMTV-Net: Automated Total Metabolic Tumor Volume Segmentation in FDG PET/CT Images

This study focuses on automating the segmentation of Total Metabolic Tumor Volume (TMTV) in lymphoma management, a crucial step for quantitative imaging biomarkers. Using a two-step cascaded approach, the research employed a dataset of 1,418 FDG PET/CT scans from four global centers. The data was divided into development/validation/test sets (900 scans) and multi-center external testing (518 scans), comprising various cancer cases, including lymphoma.

The methodology involved resampling PET/CT images into different voxel sizes, followed by training multi-resolution 3D U-Nets with 5-fold cross-validation. Ensembles of models were created, and soft voting was applied to predicted masks in the second step, utilizing probability-averaged predictions. Models were trained with a semi-supervised loss, and test time augmentation (TTA) was explored for performance enhancement.

Results indicated a significant improvement in TMTV segmentation, with an average DSC of 0.68±0.12 on the test data and 0.68±0.18 on multi-site external data, outperforming state-of-the-art methods. The approach also improved TMTV quantification, correlating strongly with the ground truth. Qualitative evaluation demonstrated agreement between quantitative results and clinician feedback.

In conclusion, TMTV-Net exhibited robust segmentation across various lymphoma subtypes and different centers, with only a slight reduction in performance on external data.

TRAINEE TALK #2

Alexandre Banks Gadbois

Master's, SBME
Supervisor: Tim Salcudean

Trainee Talk Details:

Location: LSC 1001
Time: 10:00am

Where a Surgeon Looks: Eye Gaze Tracking in Robot-Assisted Surgery

While robot-assisted minimally invasive surgery (RAMIS) offers benefits including reduced blood loss and faster post-operative recovery, it often compromises operating room efficiency, leading to extended operating times and increased strain on the medical system. To enhance surgical workflows, the literature suggests that a surgeon's point of gaze (POG) can be used to automate robotic endoscope movement. In order to achieve this, previous studies integrated an eye-gaze tracker with the da Vinci Surgical System; however, this system suffered from reduced accuracy when surgeons moved their heads and required frequent recalibrations, making it impractical for the operating room. In response, our study introduces a novel head movement compensation (HMC) algorithm that requires only a single calibration and is robust to head repositioning during robotic surgery.

The HMC algorithm extracts the user's eye corners as a proxy for head position. These eye corners are then fed as input to a model that estimates eye gaze tracking error and uses this to compensate for surgeon head movement. In a validation study involving 26 participants, our pipeline demonstrated a 2.2 mm reduction in POG error and showed minimal accuracy loss with multiple head replacements.

Our method reduces the error in POG estimation which is a first step in using eye motion to automate endoscope movement in robot-assisted surgery.

TRAINEE TALK #3

Ishika Luthra

PhD, SBME
Supervisor: Carl de Boer

Trainee Talk Details:

Location: LSC 1001
Time: 10:30am

Regulatory activity is the default DNA state in eukaryotes

Genomes encode for genes and the regulatory signals that enable those genes to be transcribed, and are continually shaped by evolution. Genomes, including those of human and yeast, encode for numerous regulatory elements and transcripts that have limited evidence of conservation or function. Here, we sought to create a genomic null hypothesis by quantifying the gene regulatory activity of evolutionarily naïve DNA, using RNA-seq of evolutionarily distant DNA expressed in yeast and computational predictions of random DNA activity in human cells and tissues. In yeast, we found that >99% of bases in naïve DNA expressed as part of one or more transcripts. In humans, we found that, while random DNA is predicted to have minimal activity, dinucleotide content-matched randomized DNA is predicted to have much of the regulatory activity of evolved sequences. Naïve human DNA is predicted to be more cell type-specific than evolved DNA and is predicted to generate co-occurring chromatin marks, indicating that these are not reliable indicators of selection. Our results indicate that evolving regulatory activity from naïve DNA is comparatively easy in both yeast and humans, and we expect to see many biochemically active and cell type-specific DNA sequences in the absence of selection.

TRAINEE TALK #4

Thristan Taberna

PhD, SBME
Supervisor: Peter Zandstra

Trainee Talk Details:

Location: LSC 1001
Time: 10:45am

Producing blood cell progenitors with T cell competence from pluripotent stem cells in scalable dynamic suspension culture

We are developing a scalable bioprocess to produce off-the-shelf T cell immunotherapies using pluripotent stem cells (PSCs). The current vein-to-vein model for chimeric antigen receptor (CAR) T-cell therapy is expensive, inaccessible, and variable. Our differentiation system generates CD34+CD43+ hematopoietic cell progenitors (HPCs) with T cell competency in dynamic suspension culture, using a serum- and feeder-free system with a favourable hydrodynamic environment. In the seed train, PSCs self-assemble via shear-controlled aggregation, which results in a 14.3±6-fold expansion and viable densities of (4.39±2) $\times 10^5$ cells/mL. A stepwise protocol mimics key blood development signals to induce blood progenitor cells, which undergo phase transformation during the endothelial-to-hematopoietic transition (EHT) process in suspension culture. The resulting CD34+CD43+ single cells have T cell competency, as demonstrated by their differentiation into CD5+CD7+ T cell progenitors with a frequency of (36.9±2) % and yield of 12.7±6 when placed in an optimized PSC-derived T cell maturation process. Ongoing studies are examining the influence of bioprocess parameters on notch signaling in aggregates and the frequency and yield of T cell competent blood progenitor cells. Our scalable approach has the potential to drive down the cost of CAR T-cell therapy and make it more accessible to patients.

TRAINEE TALK #5

Naomi Jung

Undergraduate, SBME
Supervisor: Rizhi Wang

Trainee Talk Details:

Location: LSC 1002
Time: 3:55pm

Abnormal Structures in Prostate Cancer Metastatic Bone Lesions as a Fracture Risk Factor

Prostate cancer (PC) is the most frequently diagnosed male cancer. 20% of patients develop metastatic disease ~70% of whom will suffer from PC bone metastases (PCBM). PCBM reduces quality of life due to intractable pain and high risk of fracture. This study aims to characterize the structure of PCBM-involved bone and the connection between structural changes and increased fracture risk. We evaluated the bone macrostructure and trabecular properties of 67 PCBM, and 12 control, cadaveric vertebral specimens using microCT (10 μm voxels). We performed quantitative backscattered electron SEM on a subset of 12 samples to observe microstructural details. A custom MATLAB script was used to identify lacunae density and properties in osteoblastic bone and control trabeculae. We observed 4 qualitative phenotypes using microCT: osteolytic (n=15), mixed (n=20), osteosclerotic with residual trabeculae (n=22), and osteosclerotic with minimal residual trabeculae (n=15). PC sclerotic bone had a greater lacunae density and lacunae area/bone area compared to residual trabeculae. Lacunae in PC sclerotic bone had significantly different morphological parameters and a loss of anisotropy. PCBM lesions have altered bone architecture with a primarily osteoblastic presentation, and abnormal lacunae density and characteristics. These quantitative and qualitative pathologic structural differences indicate that PCBM lesions are subjected to irregular loading of the bone that can elevate fracture risk.

TRAINEE TALK #6

Josh Friesen

PhD, SBME
Supervisor: Anna Blakney

Trainee Talk Details:

Location: LSC 1002
Time: 4:10pm

Tri-Component Polyplexes for Enhanced Delivery of Self-Amplifying RNA

Self-amplifying RNA (saRNA) is a next-generation vaccine platform, which requires a smaller dose than mRNA to induce an immune response and could reduce side effects and increase vaccine production efficiency. Like other RNA vaccines, it requires a delivery system to prevent degradation and promote cellular uptake. Many delivery systems already exist, including lipid nanoparticles (LNPs) and cationic polymers, such as pABOL, a polymer which has been optimized for delivery of saRNA. Comparisons of LNPs and pABOL saRNA vaccine delivery have shown that LNP delivery led to an overall higher immune response, while pABOL delivery induced approximately 100x higher intramuscular protein expression. These delivery systems differed mainly in their surface charge, and it has been shown that surface charge greatly impacts cellular tropism. Using biocompatible anionic polymers to neutralize pABOL polyplexes high surface charge, we aim to alter the cellular tropism and increase immunogenicity while maintaining high protein expression of pABOL polyplexes to yield highly efficient vaccine delivery systems. We have identified several polymers that successfully formulate with pABOL-saRNA polyplexes to create formulations with surface charges ranging from +15mV to -20mV with all triplexes maintaining high levels of protein expression in-vitro. In future studies we will test these formulations for their protein expression, immunogenicity, and cellular tropism in a BALB/c mouse model.