OICR
Ontario Institute for Cancer Research

IMAGING
Imaging Pathology Validation Core

MISSION AND OBJECTIVES

The Imaging Pathology Validation Core is a collaborative research platform that is focused on validation of imaging technologies and cancer biomarkers against ground truth provided by histopathology and molecular profiling. In addition to addressing internal research objectives, the IVC provides leading edge, multifaceted support to clinical trials and catalyst projects and is actively pursuing new collaborations with cancer biomarker researchers in the province and beyond.

RESEARCH INTERESTS AND EXPERTISE

The research interests of the Core are to develop imaging and digital pathology to address the needs of personalized/precision medicine. We utilize information from genomics/transcriptomics profiling and biomarker assessment to validate novel signatures that inform key decisions in risk assessment, diagnosis, characterization of cancers and treatment and monitoring of response to therapy.

Working closely with collaborators in industry, our laboratory has been exploring several approaches to biomarker multiplexing for research. In particular we have worked with two platforms, one based on multi-spectral deconvolution (MSD), the other employing a sequential-(fluorescent)-stain-bleach (SSB) approach. Each has strengths in specific areas. For example, the deconvolution method can be readily used with whole-mount slides while the SSB system allows simultaneous co-location studies of up to 60 markers on a single tissue section or tissue microarray (TMA).

We are extending our efforts from protein biomarker multiplexing to the incorporation of DNA/RNA probes. This application will be particularly useful in characterizing cancer clonal heterogeneity and grading of certain cancer types in the clinic. We work closely with the Genomics Core Facility (part of the Biomarker Imaging Research Lab at the Sunnybrook Research Institute) to conduct large-scale genomics and transcriptomics profiling research.

We have been actively developing image analysis tools and algorithms for histopathology, immunohistochemistry and biomarker multiplexing. We are building relationships with other expert groups to leverage collaborative potential, open-source repositories (e.g., ImageJ plugins), and commercial products within the laboratory (cellSens, Inform) for the segmentation of cellular compartments as well as tissue region classification (e.g., stroma vs cell groupings). We also investigate the spatial relationships between cell types both within the tumour and in the tumour micro-environment.

UNIQUE CAPABILITIES

In addition to the biomarker multiplexing capability described above, the lab has developed a full range of digital whole-mount histopathology techniques, currently producing whole organ (≤ 5" x 7") slides from breast, prostate, tongue, colorectal and brain cancer tissue samples. Work is focused on quantitative three-dimensional (3D) histopathology, imaging correlation and image processing. Several state-of-the-art digitizers are available to accommodate various sample sizes and to perform bright field or fluorescence scanning of tissue slides.

The Core at Sunnybrook offers access to imaging pathology validation services and resources for the following applications:

- Whole-mount tissue processing and large format tissue slide (up to 5"x7") preparation for validation of imaging outcomes or response to treatment;
- Advanced immunohistochemistry (whole-mount and conventional) and cross-platform image registration;
- Biomarker panel development and validation using multiplexing technologies developed by GE Global Research in combination with molecular profiling for collaborative research projects;
- Multimodality image processing and registration and algorithm development, including an internally developed multispectral platform;
- Large capacity tissue slide scanners and slide digitization;
- Next-generation sequencing capacity (Ion torrent and IonS5 Systems) for high-throughput profiling of targeted panels or whole-exome molecular changes in short timeframes.

We work with Dr. Jean Gariepy on a aptamer platform that can flexibly create highly specific, inexpensive new imaging probes for testing of immunogenicity, grading, etc.

The laboratory is accredited under IQMH (formerly OLA) and has implemented clinical standards for quality control and process monitoring including clinically compatible tissue tracking system.

Our development of 3D pathology techniques for the prostate includes software modules for reconstruction of serial pathology sections and MR images. These modules improve the registration accuracy by using a method that reintroduces 3D information lost during histology processing.

The software module for reconstruction of serial pathology sections uses a mutual information metric to align an image with the next in the stack. Our algorithm allows reconstruction of a volume less than 500 MB in size.

A software module is available to allow real-time manipulation of very large 3D images typically generated in 3D digital pathology to provide the user with a multiresolution environment to view a 500 GB image and select a sub-volume region of interest that can be loaded into the PC's memory for real-time viewing. The user would then be able to move the sub-volume within the larger volume, interactively.

Other capacities include development of study designs, selection and optimization of immunostaining, quality control processes, access to clinical specimens, image and sample tracking databases, and pathology consultations.

TRACK RECORD

The Core is a mature cutting edge platform developed with OICR's support since 2007. Some of the highlights of current and past collaborations include:

- Immunohistochemistry and data analysis for a clinical trial of the Canadian Atherosclerotic Imaging Network, PI: Dr. Jean-Claude Tardif;
- Whole-mount breast mastectomy and lumpectomy trials;
- Whole-mount histopathology services to the Terry Fox Imaging Program Photoacoustic Imaging Of Prostate Cancer In *Ex Vivo* Post Prostatectomy Specimens, PIs: Dr. Masoom Haider and Dr. Brian Wilson;
- Clinical trial on Correlation of FAZA PET hypoxia Imaging to 3D Histology (FAITH) in oral tongue cancer, PI: Dr. Ian Poon;
- Validation of imaging findings in a pilot Hyperpolarized 13C prostate clinical trial, PI: Dr. Charles Cunningham;
- Planned pancreas imaging clinical trial, PI: Dr. Masoom Haider;
- Several collaborative projects with the Anatomic Pathology department at Sunnybrook and other institutions on various applications for cancer biomarkers multiplexing.

CONTACT INFORMATION

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Ontario

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