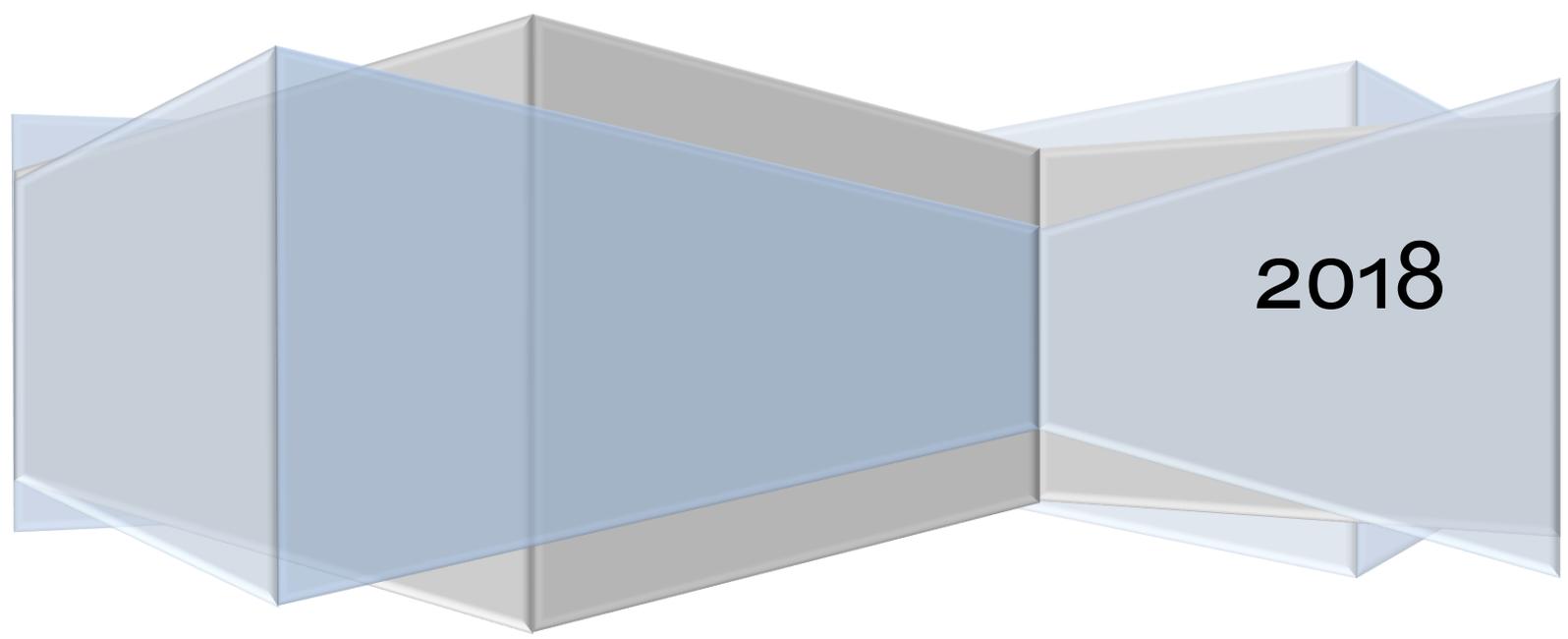


Global Engage's

# 4th Digital Pathology Congress: USA

Poster Presentation Abstracts  
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Poster Title	Distinction of Benign and Malignant Breast Histology Through Deep Learning
Abstract	<p>Background:</p> <p>Breast cancer is the most common cause of cancer in women. Treatment modalities depend on the stage and type of cancer and include surgery, radiation, and chemotherapy. Conventionally, a pathologist evaluates a tissue section slide under a light microscope and renders a benign or malignant diagnosis based on the structural patterns seen. Advances in machine learning technologies have demonstrated deep learning as a flexible and powerful tool in the classification of histopathological images, making it a viable tool for pre-screening breast cases for malignancy. Pathologists can be alerted of the presence of a potentially malignant case, paving the way for earlier diagnosis and treatment.</p> <p>Design:</p> <p>A set of 72 benign and 72 malignant images taken at 3 different magnifications were procured from a previously published study<sup>1</sup>. Each image was assigned to either of two classes- benign or malignant. VGG-16(an open source deep learning algorithm) in combination with Random forest and other machine learning algorithms was used to train a machine learning model for predicting which class each image belonged to. Model performance was evaluated using 10 -fold cross validation and random sampling of the dataset, with a training set size of 70% of the image collection.</p> <p>Results:</p> <p>Evaluation through 10 -fold cross validation and random sampling using a training set size of 70% yielded ROC AUC scores of approximately 0.96 and classification accuracies of approximately 0.91. 8 out of 72 benign cases were misclassified as malignant. 5 out of 72 malignant cases were misclassified as benign.</p> <p>Conclusion:</p> <p>Convolutional neural networks are useful for identifying malignant breast lesions and hold promise as an adjunct to the slide screening process.</p> <p>References:</p> <p>1. Levenson RM, Krupinski EA, Navarro VM, Wasserman EA. Pigeons (<i>Columba livia</i>) as trainable observers of pathology and radiology breast cancer images. PLoS One 2015;10:e0141357.</p>

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Poster Title	Biomarker Colocalization Analysis of a Virtual 12-plex using Discovery Chromogenic Dyes and Tissuealign™ Co-registration Software
Abstract	<p>New Chromogenic Dyes from Ventana Discovery combined with Visiopharm's Tissuealign™ produce highly multiplexed virtual images (8-, 10-, 15-plex or more). Spatial overlap of these new chromogens in a tissue section will result in the formation of a third color representing biomarker colocalization (e.g. Yellow plus Purple make Orange). The source of chromogens forming color combinations can become confounding if staining varies, ratios of overlapping colors differ, or as more colors accumulate and darken. Here we test cellular biomarker colocalization after superimposing serial sections with Tissuealign™. Three tonsil tissue sections cut at 4-micron intervals were stained with Discovery Purple CD8 plus combinations of Discovery Teal, Discovery Yellow Ki67, and hematoxylin counterstain, then digitized and co-registered using Tissuealign™. Over half of the Discovery Purple CD8 positive cells had overlapping CD8 signal in the adjacent serial section and 93% in at least one section when both flanking sections are present. 74% of the CD8 signal in the center section had overlap throughout the three sections. But 14% of CD8 signal detected in the two edge sections was not contiguous through the center section, suggesting overlapping signal could be from coincident neighbouring cells in some cases. We conclude that Virtual Multiplexing can be used for biomarker colocalization between neighbouring sections because we were able to detect the same biomarker with overlap in neighbouring sections, with the caveat that the cellular size and sectioning intervals are within range for such detection.</p>

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Poster Title	A deep learning-based model of normal histology
Abstract	<p><b>Background:</b> Several deep learning models, trained on pathologies in various tissues, have been reported in the literature. However, these models are all specific to a certain tissue/context. A layer describing the diversity of normal tissues could be an ingredient of a more generic approach.</p> <p><b>Objective:</b> To establish a model of normal tissue, as a foundation for future models of histopathology.</p> <p><b>Methods:</b> On 449 slides scanned at 40x (0.25 microns/pixel), representing various tissues from normal rats (<i>Rattus norvegicus</i>), tissue regions were outlined and annotated by pathologists according to two taxonomies of different detail (7 and 23 classes, respectively). From these regions, a total of ~800,000 small patches of 224x224 pixels were generated at various levels of resolution down-sampling.</p> <p>For each combination of tissue taxonomy and down-sampling level, a VGG-16 neural network was trained using a transfer learning approach, with weights pre-initialized via the ImageNet dataset, followed by fine-tuning on our training dataset of tissue patches.</p> <p>The final fully connected layer of the VGG-16 network constitutes a learned representation (encoding) of a given image patch. Patterns formed by the entirety of image patches in the encoding space were analyzed using the t-SNE dimensionality reduction method.</p> <p><b>Results:</b> Model accuracy ranged from 94.5% to 98.2% on the validation datasets. Increasing accuracy was observed with increasing down-sampling level and more detailed taxonomy. In an assessment of the misclassified patches, unequivocal tissue identification was often impossible for expert pathologists as well. The t-SNE visualization of the encoding space revealed pronounced, mostly non-overlapping clusters corresponding to individual tissue classes.</p> <p><b>Conclusions:</b> Accurate tissue type classification from small image patches can be achieved using “off-the-shelf” neural network architectures. Segmentation of tissue regions on a whole slide will be possible at even higher accuracy, as misclassifications made on some patches can be “outvoted” by classifications on adjacent or overlapping patches at various resolution down-sampling levels.</p>

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Poster Title	Paradox of Exclusion of Most Interesting Futuristic Subjects from Meeting Programs and Summit Papers
Abstract	<p>In the past when there were fewer modes of communication physicians could rely upon national and international meeting programs to alert them to new areas of scientific inquiry they should explore to keep up with developments in their field. Similarly summit papers and reviews in the medical literature could be counted on to include new information about evolving areas of the discipline in question the reader should explore. With the advent of social media and its myriad of new communication modes this is no longer true and physicians who rely on only old fashioned traditional means of keeping up with their field are at significant risk of being blind-sided by new developments they know nothing about. Whether it is intentional and overt or accidental and subconscious, those areas of science being actively pursued by the major funders of meetings tend to be highlighted in meeting programs and summit paper reviews whereas other subjects less in the funding mainstream are excluded. For instance the Global Kidney Disease Summit of 2017 published in Kidney International and the Lancet in October 2017 had not a single reference or mention of these terms which are central to the future of kidney disease research: "repair", "ex vivo perfusion", "regenerative medicine", "tissue engineering", "artificial intelligence", "artificial organs", "xenotransplantation", "human cell atlas". The conflict of interest disclosures show that the authors have many financial connections with traditional pharma and dialysis companies, no links to regenerative medicine companies or entities. The excluded subjects are central to the future of medicine. Organizers of major medical meetings and summit papers should become social media savvy and assure that all relevant subjects are included in future meetings and summit paper reviews. Promising subjects on which the future of medicine will rely cannot be excluded from meeting programs and summit paper reviews.</p> <p>Here is a YouTube video that explains the concept of the abstract further <a href="https://www.youtube.com/watch?v=dAb6EpwpEkM">https://www.youtube.com/watch?v=dAb6EpwpEkM</a></p>

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Poster Title	Truthful Promotion of Pathology and Nonfictional Models of the World for Training Sentient AI
Abstract	<p>Recently pathology has gone from having the least appealing promotional material to having perhaps the most-appealing promotional material of any medical specialty. The promotional videos at the recent 2018 USCAP meeting in Vancouver and recent issues of The Pathologist show how far we have come. To some extent these advances have been at the expense of the truth, with pleasant assurances given that artificial intelligence will result in no work force downsizing. More and more of the words we read are written by people directly employed by companies supplying products to pathologists, rather than by pathologists themselves.</p> <p>When machines are as smart as we are they will need a model for the world on which to base decisions. Our corporate partners stand ready to provide machines with a fictional world that works to their financial advantage, a kind of Fox News for sentient AI. Ethical morally-upright pathologists need to work together with sentient machines to counter these efforts to create false models of the world. This job of creating a truthful model of the world for the training of sentient AI working together with machines will be the most important job a pathologist can have in the future. The future happiness of the world depends on our getting this task right.</p> <p>Far from being a problem for the future only, there is evidence that these fictional worlds are being created today. Reasonable well-argued book discussions about AI are being repackaged for the masses with flawed dogmatic statements that even the laziest human does not have to worry about job loss to a machine. Humanness itself is absolute protection. AI will only make our lives better. Already today we need to guard against these comforting flawed versions of reality, and work to disseminate the truth in an accessible way.</p> <p>Here is a YouTube video that explains the concept of the abstract further <a href="https://www.youtube.com/watch?v=ApXIWyCzPsU">https://www.youtube.com/watch?v=ApXIWyCzPsU</a></p>

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Poster Title	Automatic detection of slides to rescan for whole slide imaging scanner
Abstract	<p>The whole slide imaging scanner(WSI) scans pathological specimens to produce digital images for pathology practice, research and computational pathology which enables monitor-based diagnosis and image analysis. However, sometimes the scanner failed to produce sufficient quality images due to focus error and noise. Insufficient quality images pose a potential risk for diagnosis and unproductive for analysis. Therefore, it is necessary to evaluate the quality of the scanned image and rescan the slide if the quality is not satisfactory. In the previous work, referenceless quality evaluation method was proposed to evaluate scanned image quality but tissue artefacts (i.e. air-bubble and tissue-fold) would also be detected as false positives. Tissue artefacts hide information and are useless for analysis and diagnosis. We proposed a method to evaluate scanned image by eliminating tissue artefacts in order to detect slides necessary to rescan for the practical use of WSI scanner. Firstly, we detected tissue artefacts using the machine learning technique. Then estimated the quality of the image based on the sharpness and noise measurement except the detected artefacts and glass area. Quality was estimated by diving the whole slide images into fixed size blocks. We detected the glass area based on the number of white pixels in a block. Finally, the quality of the whole slide image was estimated from the quality of evaluated blocks. Through the experiments, the effectiveness of the proposed method was confirmed. The method was demonstrated for differently stained slides (i.e. HE, IHC, PAS) of major tissue organs (i.e. heart, liver, lung, intestine) which were scanned by two different scanners.</p>

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Poster Title	Preliminary Studies in the Use of the Foldscope Paper Microscope for Diagnostic Analysis of Crystals in Urine: Issues in the Analysis of Liquid Samples and Potential Applications in Low Budget/Low Tech Regions of the World
Abstract	<p>The Foldscope was developed by Dr. Manu Prakash at Stanford as a cheap (under \$1.00) microscope made of paper and usable for microscopy by students all over the world and in more serious research or diagnostic roles by professionals. It is especially advantageous to those in regions of the world where budget and availability of high-end instrumentation is severely limited. Here at NYCPM, we obtained a Foldscope from Dr. Prakash. We assembled it ("fold on the dotted lines"), inserted battery and lens and produced a microscope. Two of us (RC and DS) had prior certification and experience as laboratory technicians, including urinalysis. It was determined to evaluate if the Foldscope could be used in this role. Preliminary projects were designed to test this, by preparing samples of likely target crystals – uric acid and calcium oxalate. This was preliminary, as real urine samples from real patients required complex IRB approval, rules and regulations. In this study, it was determined that the crystals could in fact be visualized with this low budget instrument. Furthermore, several issues emerged, different from using a glass or digitized slide – e.g., holding the microscope up to a light source resulted in the liquid sample dripping on the observers face (!). Methods were developed to keep it flat, with attention to clamps to hold it and a light source appropriately placed. Successful imaging by iPad or cell phone allows the necessary component of Telepathology implicit in its application. Further development is needed as to methodology and as to validation with patient samples. Determination of the full range of identifiable crystals and cells of diagnostic significance would expand the usefulness of this application. Its use in low budget/low tech regions of the world would be greatly advantageous.</p>

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Poster Title	Toward the Automation of Fluorescence In Situ Hybridization (FISH) Scoring Using a Confocal Whole Slide Image Scanner and Image Analysis Software.
Abstract	<p><b>Introduction</b></p> <p>The standard, manual scoring for fluorescence in situ hybridization (FISH) is labor-intensive and time-consuming. Confocal imaging which eliminates out-of-focus noise offers higher resolution and more spatial information than conventional widefield imaging. The purpose of this study was to establish the automated FISH scoring method using a confocal whole slide image (WSI) scanner and image analysis software which is commercially available.</p> <p><b>Materials and methods</b></p> <p>Six archival break-apart FISH slides were prepared for the current study (four negative slides and two positive slides clinically). Several regions of interest (ROIs) were selected for confocal scanning according to the corresponding H&amp;E and immunohistochemistry slides. FISH slides were digitized by a Panoramic Confocal WSI scanner (3DHistech Ltd., Budapest, Hungary) with a 40x water immersion objective (0.1625 micrometer/pixel). We scanned seven layers at 0.6 µm intervals based on the optimization results of the previous study. The images were viewed in CaseViewer (3DHistech), and ROIs for image analysis were defined. The image analysis for FISH scoring was performed with Imaris (Bitplane, Zurich, Switzerland), in which we created algorithms for nuclear segmentation, spot quantification and detection of spot co-localization. The accuracy of the analysis was assessed by a pathologist.</p> <p><b>Result</b></p> <p>Confocal scanning of FISH slides provided sharp images with spatial information of spot signals. By our semi-automated algorithms in Imaris, nuclear segmentation and spot detection were successfully performed. The ratio of rearrangement signals were correlated with the clinical results.</p> <p><b>Conclusion</b></p> <p>We established the semi-automated method of FISH scoring combined with confocal scanning. This method was helpful to obtain accurate, plentiful information of FISH more efficiently than conventional manual methods. The next step is to enrol more clinical cases for evaluation and validation. Furthermore, according to the protocol and the data of this study, we are currently developing in-house software for the fully automated FISH scoring system also considering deep learning.</p>

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Poster Title	Machine learning approach to tumor immune infiltrate analysis from H&E images
Abstract	<p><b>Objective:</b> Develop a scalable, automated method to quantify immune cells in H&amp;E-stained breast cancer images.</p> <p><b>Hypothesis:</b> Staining serial sections of tumour tissue by H&amp;E and CD45 immunostaining is a robust and scalable alternative to obtaining expert-annotated ground-truth data for training algorithms that detect immune cells.</p> <p><b>Approach:</b> We performed H&amp;E and CD45 IHC staining on sequential sections of a breast cancer tissue microarray and trained a neural network to predict average IHC staining levels. We subsequently validated the model on a publicly available dataset of H&amp;E stained breast cancer images that were annotated by a pathologist (100 patients, 3064 identified lymphocytes). We evaluated whether algorithm-predicted immune quantification from H&amp;E is associated with survival in a cohort of 353 breast cancer patients.</p> <p><b>Results:</b> The algorithm shows high correlation with the pathologist-annotated dataset (<math>R=0.65</math>, <math>p&lt;10^{-5}</math>). High immune infiltrate predicted by the neural network is associated with longer survival (<math>p&lt;0.001</math>).</p> <p><b>Conclusion and Future Work:</b> We demonstrate a simple and powerful approach to train classifiers to identify cell types from H&amp;E images. We plan to scale this approach to additional immune marker types (e.g. CD3, CD20, CD68), and use the predictions from the neural network to relate immune cell counts and spatial distributions to clinical outcome.</p>

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Poster Title	Vulcan – Novel Digital Pathology System for multi-specimen analysis using spectral and spatial imaging
Abstract	<p>Vulcan digital pathology system is a fully automated microscope, to image cancer biopsies, blood smears and pap smears; convert them to high quality digital images; present a seamless workflow to the pathologist so that they don't miss their manual microscope; and to provide an array of mathematical tools to help them generate accurate and consistent reports – from their lab, or from anywhere in the world.</p> <p>Our differentiator is a complete re-think of how these digital pathology systems are built traditionally. Digital Pathology has become synonymous with Biopsy imaging. Whereas, a microscope is also used for several tests in a pathology lab – blood samples, pap smears, sputum samples, body fluids, bacteria cultures, etc. Normal diagnostic labs can't embrace digital pathology for a 10% workload which may be biopsies and keep the status quo on the rest. They can't take advantage of the efficiencies from digital, and transform their resource planning. There is no system in the world today that aims to convert all of their workflow to digital with a single box.</p> <p>We are aiming to change this paradigm with our Vulcan digital system. One piece of hardware in the lab can be repurposed with a click of a mouse button to deal with any of the samples above. We have built innovative algorithmic pipelines for dealing with these various types of specimens. And have built it as one of the most affordable systems in the world through extensive reliance on the concept of software-hardware co-design. Our aim is not to build a personal device for screening in a health camp or for in-home use; we have built a clinical grade system that provides a pathologist the confidence to write a report.</p> <p>Our proprietary hyperspectral camera is one of the most affordable spectral imaging systems available, which allows us to simultaneously capture RGB and Spectral images of the specimens. With this additional data, we are building advanced AI pipelines. This poster will demonstrate our solution for completer peripheral blood smear analysis – RBC, WBC, Platelet morphology analysis. Simultaneously, the poster will demonstrate our solutions for Lung Fibrosis detection, Dermatology quantitative analysis for Psoriasis, and several other applications.</p>

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Poster Title	The Roles of Micro-Computed Tomography (CT) in Breast Pathology
Abstract	<p>Background: Breast cancer spreads by contiguous stromal invasion and also by intraductal proliferation with possible noncontiguous invasion. Intra-operative evaluation of surgical margin is advocated to reduce the re-excision rate and local recurrence, but sampling error or skip lesions may limit the assessment. Micro-CT enables the study of the 3D structure of the tissue and does not require any tissue sectioning or loss of sample. We evaluated micro-CT images of fresh breast tissue and lymph nodes, and compared the findings with those in micro-CT of formalin-fixed paraffin embedded (FFPE) tissue blocks with available hematoxylin-eosin (H&amp;E) stained sections.</p> <p>Design: Fresh tissue samples of breast and lymph node tissue were scanned using a custom-built micro-CT scanner (Nikon Metrology). We aimed to complete micro-CT scanning of fresh tissue slices within 5 minutes so that it would be feasible for intraoperative evaluation. Micro-CT scanning of FFPE tissue blocks aimed to give the best resolution. All H&amp;E slides were scanned at 20x by Aperio AT2 (0.5um/pixel). We then investigated the correlation between micro-CT images and histology.</p> <p>Results: In micro-CT images of fresh tissue carcinoma as an expansive high density area; ill-defined invasion into fat appears as a diffuse ground glass opacity. Micro-CT evaluation of benign and metastatic lymph nodes has lower resolution. Micro-CT of FFPE blocks highlighted the structure of intramammary carcinoma and normal breast tissue, lymph node metastases, but detection of the cellular composition within the breast ducts remains a challenge.</p> <p>Conclusion: Micro-CT imaging shows possible applications for the intra-operative assessment of invasive carcinoma in surgical margin. Correlation between micro-CT images of FFPE blocks and histology suggested a potential for detecting pathologic features and tumor spreading without histology slides. Further investigation is ongoing to use micro-CT for intraoperative evaluation, particularly with regard to possible scanning of the entire lumpectomy specimen, without sectioning, and image analysis.</p>

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Poster Title	PathologyMap: A New Tool for Preclinical Cancer Research
Abstract	<p>Introduction: Currently there is no large centralized online Whole Slide Imaging (WSI) repository for histopathology data, making collaboration difficult and bioinformatics-driven discovery impossible. We wanted to know if it was possible to build a self-sustaining, crowd-sourced digital pathology database for cancer research discovery. Methods: HistoWiz automates histology for cancer researchers guaranteeing a 48-hour turnaround from tissue specimen to digital slides in the cloud. This system feeds digital data into an intelligent tissue platform, PathologyMap™. which employs a novel image-tagging technology to capture metadata from users and is searchable on the annotation fields. Results: Currently there are over 50,000 scanned slides and the database is growing at 220% per year. PathologyMap also reflects the current focus of cancer therapy. For instance, there are 133 slides stained for EGFR most likely related to a focus on precision medicine in the treatment of tumors. There are 1,233 slides stained for CD8 representing an increased focus on the immune microenvironment in cancer research.</p> <p>Conclusions: PathologyMap™ is the world's largest, most comprehensive Whole Slide Image (WSI) database. It not only allows for online viewing, sharing, archival, annotation, search and meta-analysis of cancer tissue images, but also access to the corresponding cancer tissue specimens. By using machine learning (ML) algorithms and allowing histology service users to contribute, annotate and compare cancer tissue data across different laboratories and hospitals around the world, PathologyMap™ will be vital for improving cancer diagnosis, discovering insights to advance cancer research, saving money by reducing repetitive research, and accelerating drug development.</p>

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Poster Title	Quantitative spatial analysis of single or multiplexed biomarkers on whole slide digital pathology images in a hospital-based multi-modality core facility
Abstract	<p>The STTARR Innovation Centre is a full-service multi-modality preclinical imaging core facility serving the preclinical imaging and image analysis needs of academic and industry partners. Part of the Princess Margaret Cancer Centre, and located in the MaRS Centre in downtown Toronto, we provide access to small animal imaging instrumentation for micro-PET, SPECT, CT, MRI, with on-site correlative autoradiography and histopathology, as well as novel modalities like imaging mass cytometry and DESI mass spectrometry. Over the past several years we have developed a number of quantitative analysis methods for digital image segmentation and classification, for identification of biomarkers across a broad range of diseases including cancer, heart disease, transplant rejection, inflammatory processes, radiation-induced tissue fibrosis, among others. Working closely with UHN pathologists, we develop and validate digital pathology algorithms to identify and measure tissue regions, cell populations, and markers of interest within tissue slides, as well as building registration tools to match pathology results with 3D imaging modalities, to address the basic and translational science questions being addressed by our researchers and clinical trials. The use of machine learning, convolutional neural networks and AI-based approaches will increasingly be needed to handle and interpret the large amount of data produced in digital pathology workflows. These methods all require large amounts of training data to be effective; to that end we are working on an image processing pipeline to mine the large number of manual annotations we have generated over the past 5 years of digital pathology analysis services, in order to develop and train next generation tissue and cell segmentation utilizing these new applied statistical methods. Our goal is to build a suite of quantitative single cell methods to perform "tissue cytometry", bringing flow cytometry style analysis to tissue sections, but incorporating additional information about spatial relationships between cellular subpopulations. Using these tools we can extract quantitative image-derived features in a reproducible and robust fashion, providing clinicians and biological scientists with tools to measure previously inaccessible phenomena, like measuring the hypoxic gradient directly within tumor sections, or comparing glucose uptake to lactic acid production in the same tumor sample.</p>

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Poster Title	Multimodal image analysis: relationship between pathological image and microscopic ultrasound image
Abstract	<p>In neurosurgery, surgeons try to identify tumor regions based on visual characteristics such as color and texture and physical characteristics, i.e., stiffness in addition to the prior information on the location of tumor region based on CT and/or MR images. In some cases, intraoperative frozen section diagnosis of the target region is also performed to confirm its location. This pathological diagnosis requires more than ten minutes and thus only a limited number of this diagnosis can be carried out. Understanding the relationship between pathological image and other modalities may lead to a solution for this problem. For example, ultrasound signals can be easily obtained during surgery and may provide effective information to meet the above need. This paper presents a preliminary study on the relationship between image features of pathological image (PT) and ultrasound signals captured with a scanning acoustic microscope system (SAM) as a cell-level analysis. In the experiment, thinly sliced specimens of glioma tissues were first prepared. Physical properties are obtained as two-dimensional ultrasonic (US) images. Then, the specimens were stained with hematoxylin-eosin and those microscopic optical images were captured. Image size and pixel size of PT image were approximately <math>12000 \times 12000</math> pixels and <math>228 \times 228 \text{ nm}^2</math>, respectively. On the other hand, those of US Image were <math>300 \times 300</math> pixels and <math>8.0 \times 8.0 \text{ }\mu\text{m}^2</math>, respectively. These two images were registered first. Microvascular was extracted manually on PT image and a percentage of microvascular region in each small window region was calculated with a size of <math>512 \times 512</math> pixels. Averaged speed of sound was also calculated in the corresponding region of US image. The correlation between those values was <math>R^2 = 0.73</math> in the coefficient of determination. This preliminary result suggests the possibility of use of US image during neurosurgery for rapid diagnosis.</p>