Spatio-temporal Sensor Integration, Analysis, Classification or

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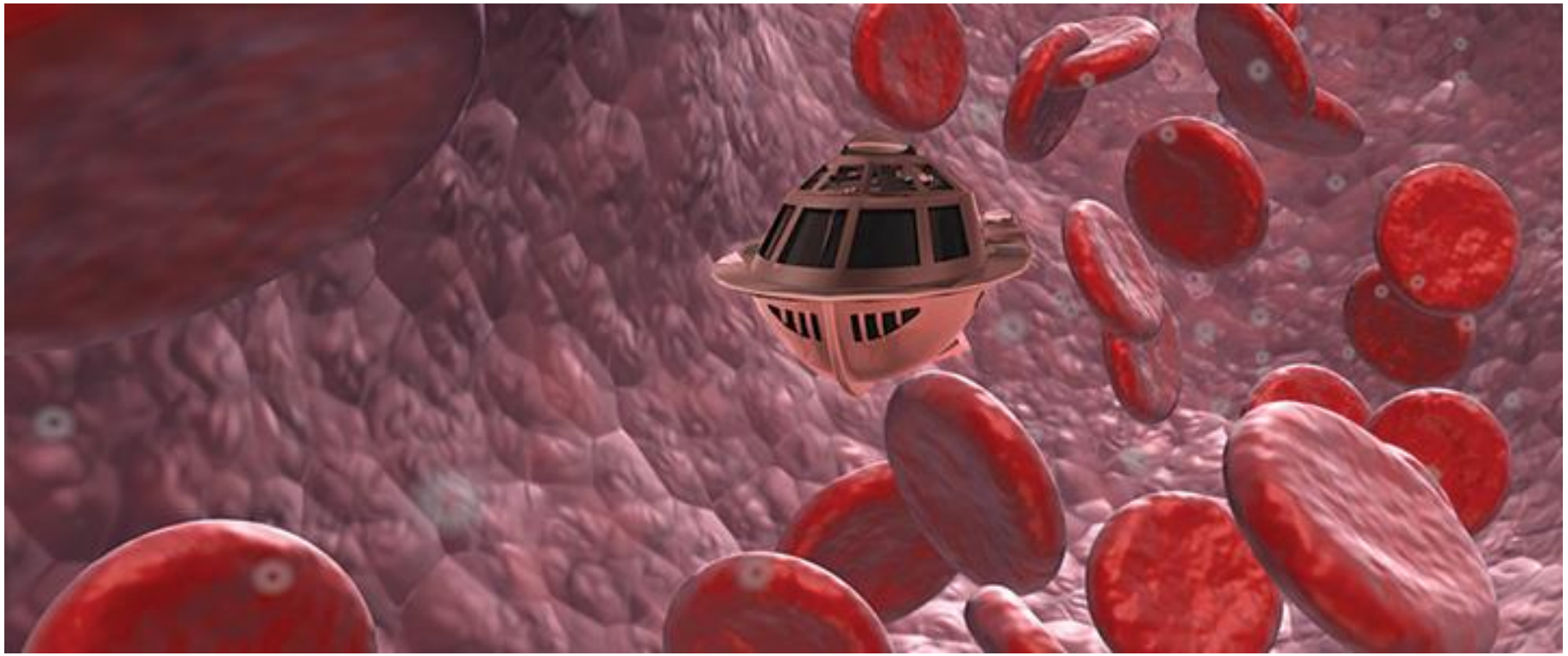


Can Exascale Cure Cancer?

Clusters, Clouds, and Data for Scientific Computing

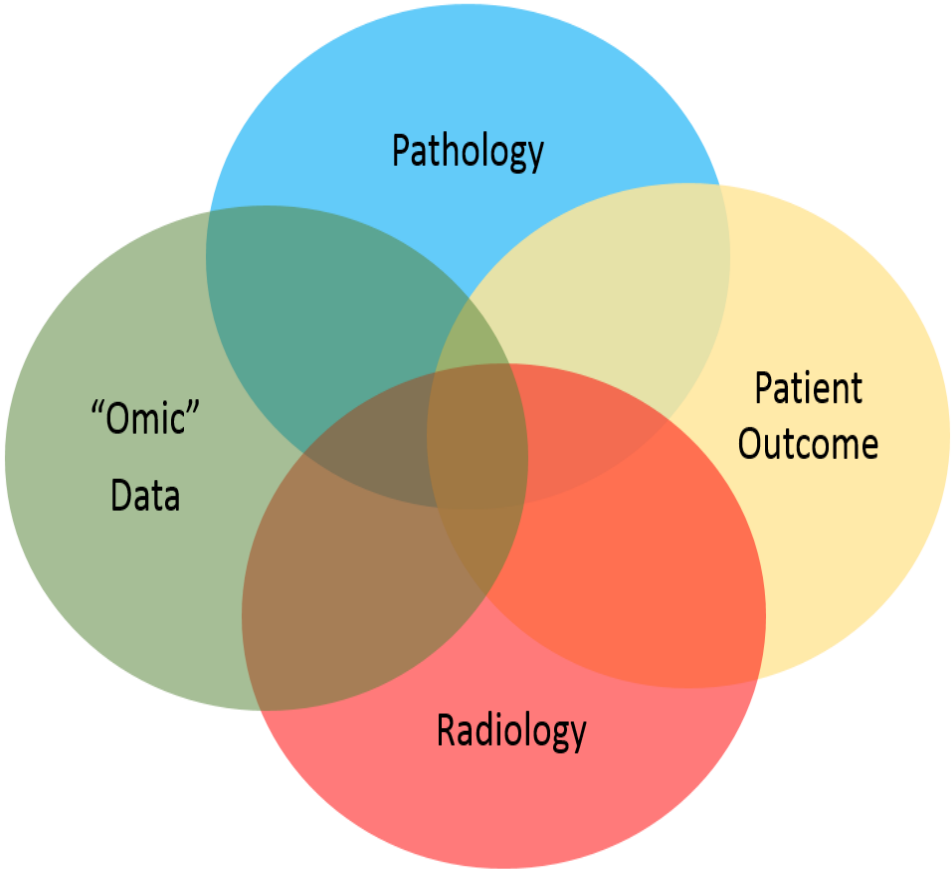
CCDSC 2014

September 2nd – 5th, 2014

Multi-scale Integrative Analysis

Stony Brook University

- ***Predict treatment outcome, select, monitor treatments***
- Computer assisted exploration of new classification schemes
- Tumor heterogeneity, Immune response
- Reduce inter-observer variability in diagnosis



Pathomics, Radiomics

Stony Brook University

- Identify and segment trillions of objects – nuclei, glands, ducts, nodules, tumor niches … from Pathology, Radiology imaging datasets
- Extract features from objects and spatio-temporal regions
- Support queries against ensembles of features extracted from multiple datasets
- Statistical analyses and machine learning to link Radiology/Pathology features to "omics" and outcome biological phenomena
- Principle based analyses to bridge spatio-temporal scales – linked Pathology, Radiology studies

FDA News Release

FDA allows marketing of first whole slide imaging system for digital pathology

For Immediate Release April 12, 2017

Release

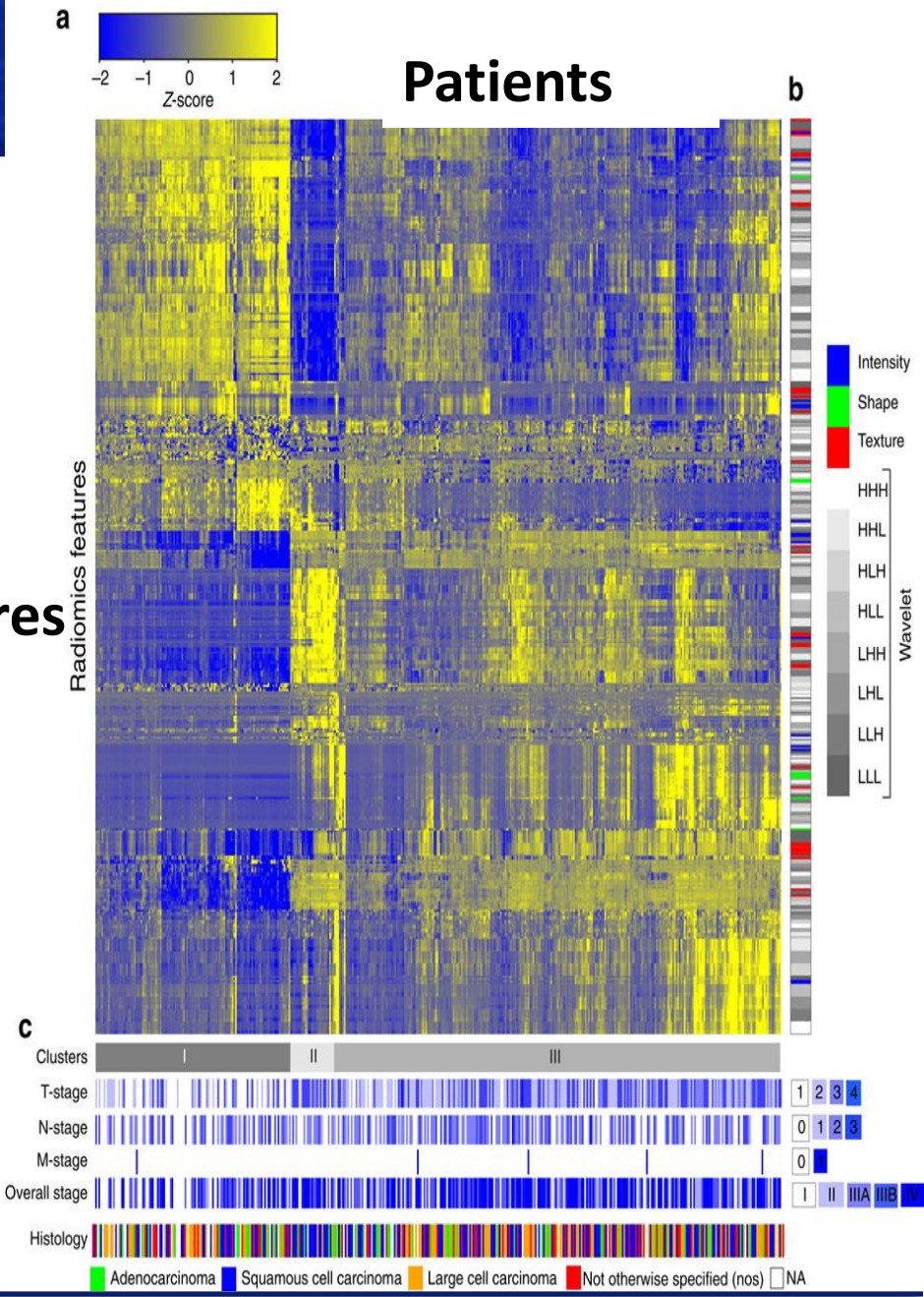
The U.S. Food and Drug Administration today permitted marketing of the Philips IntelliSite Pathology Solution (PIPS), the first whole slide imaging (WSI) system that allows for review and interpretation of digital surgical pathology slides prepared from biopsied tissue. This is the first time the FDA has permitted the marketing of a WSI system for these purposes.

Radiomics

Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach

Hugo J. W. L. Aerts et. Al.

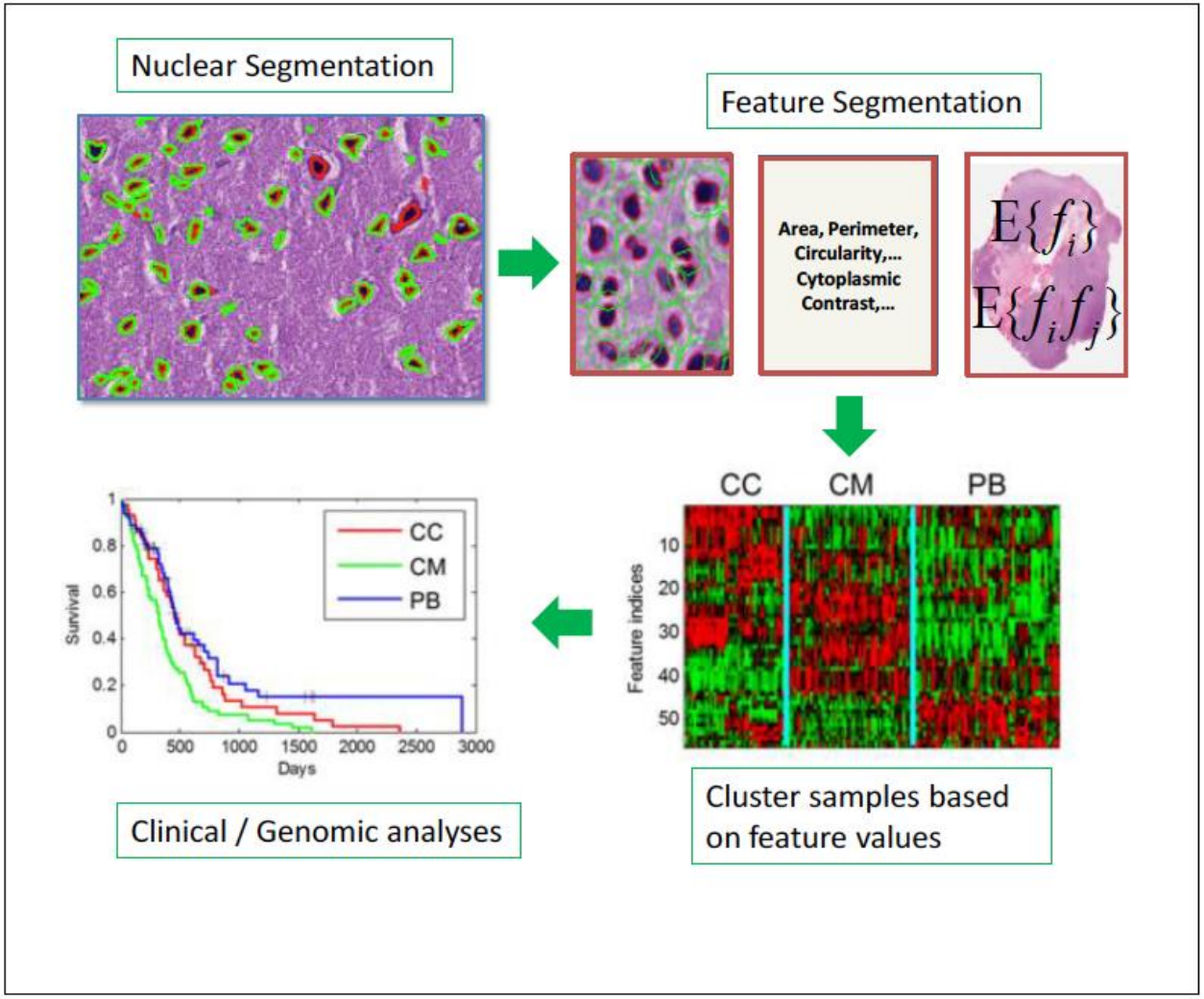
Nature Communications **5**, Article number: 4006
doi:10.1038/ncomms5006



Pathomics

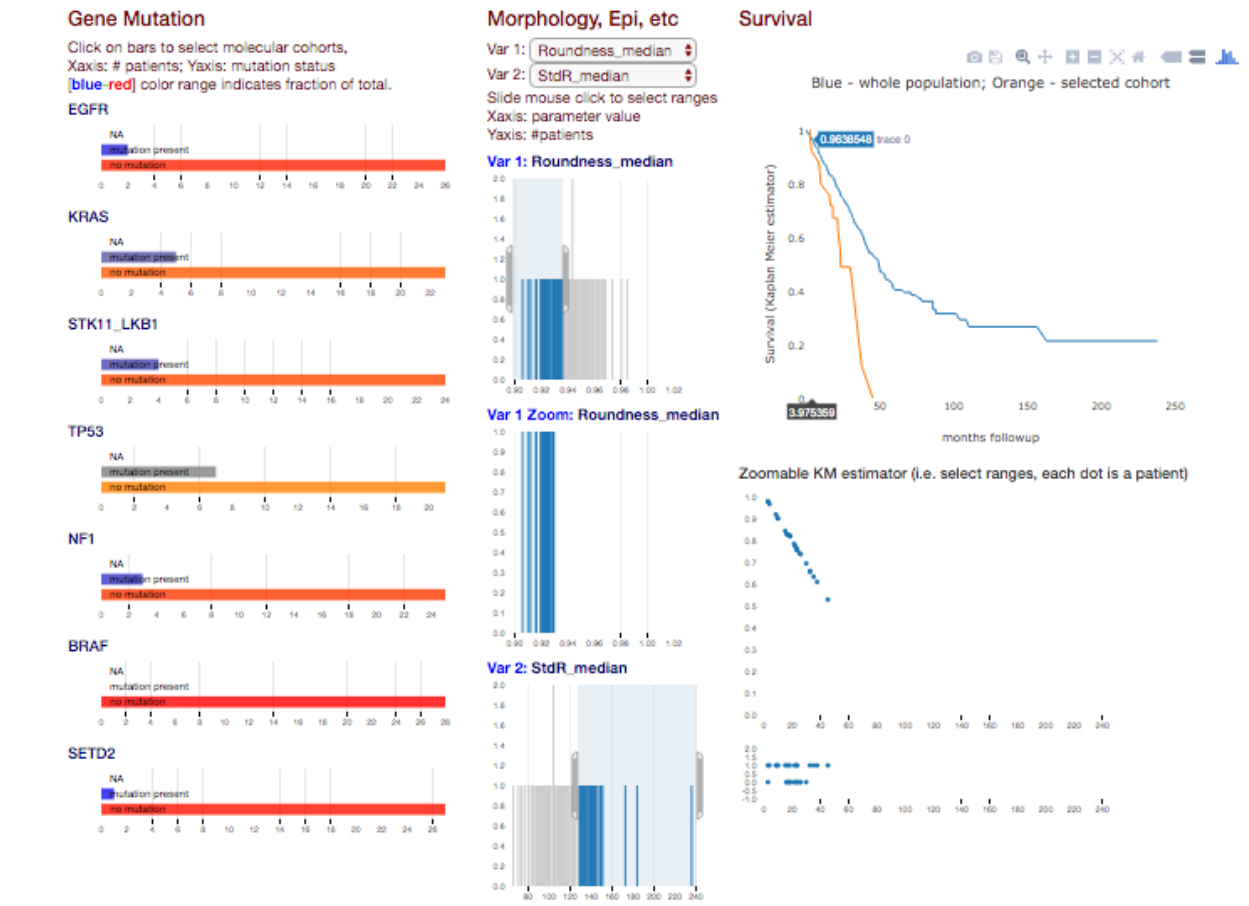
Integrative Morphology/"omics"

- Quantitative Feature Analysis in Pathology: Emory In Silico Center for Brain Tumor Research (PI = Dan Brat, PD= Joel Saltz)
- NLM/NCI: Integrative Analysis/Digital Pathology R01LM011119, R01LM009239 (Dual PIs Joel Saltz, David Foran)
- J Am Med Inform Assoc. 2012 **Integrated morphologic analysis for the identification and characterization of disease subtypes**.



Feature Explorer - Integrated Pathomics Features, Outcomes and "omics" – TCGA NSCLC Adeno Carcinoma Patients

Stony Brook University



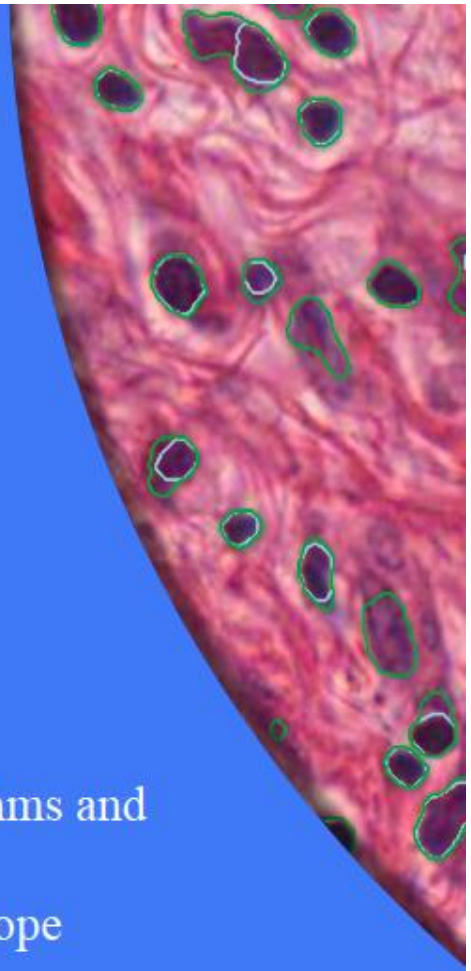
SEER Virtual Tissue Repository

- Lynne Penberthy MD, MPH NCI SEER
- Ed Helton PhD NCI CBIIT Clinical Imaging Program
- Ulrike Wagner CBIIT Clinical Imaging Program
- Radim Moravec NCI PhD, NCI SEER
- Ashish Sharma PhD Biomedical Informatics Emory
- Joel Saltz MD, PhD Biomedical Informatics Stony Brook
- Tahsin Kurc PhD Biomedical Informatics Stony Brook
- Georgia Tourassi, Oak Ridge National Laboratory

Vision – Enable population/epidemiological cancer research that leverages rich cancer phenotype information available from Pathology tissue studies

NCIP/Leidos 14X138 and HHSN261200800001E - NCI

SEER Virtual Tissue Repository



Pilot project that captures the core functionalities and processes needed in a Virtual Tissue Repository for SEER

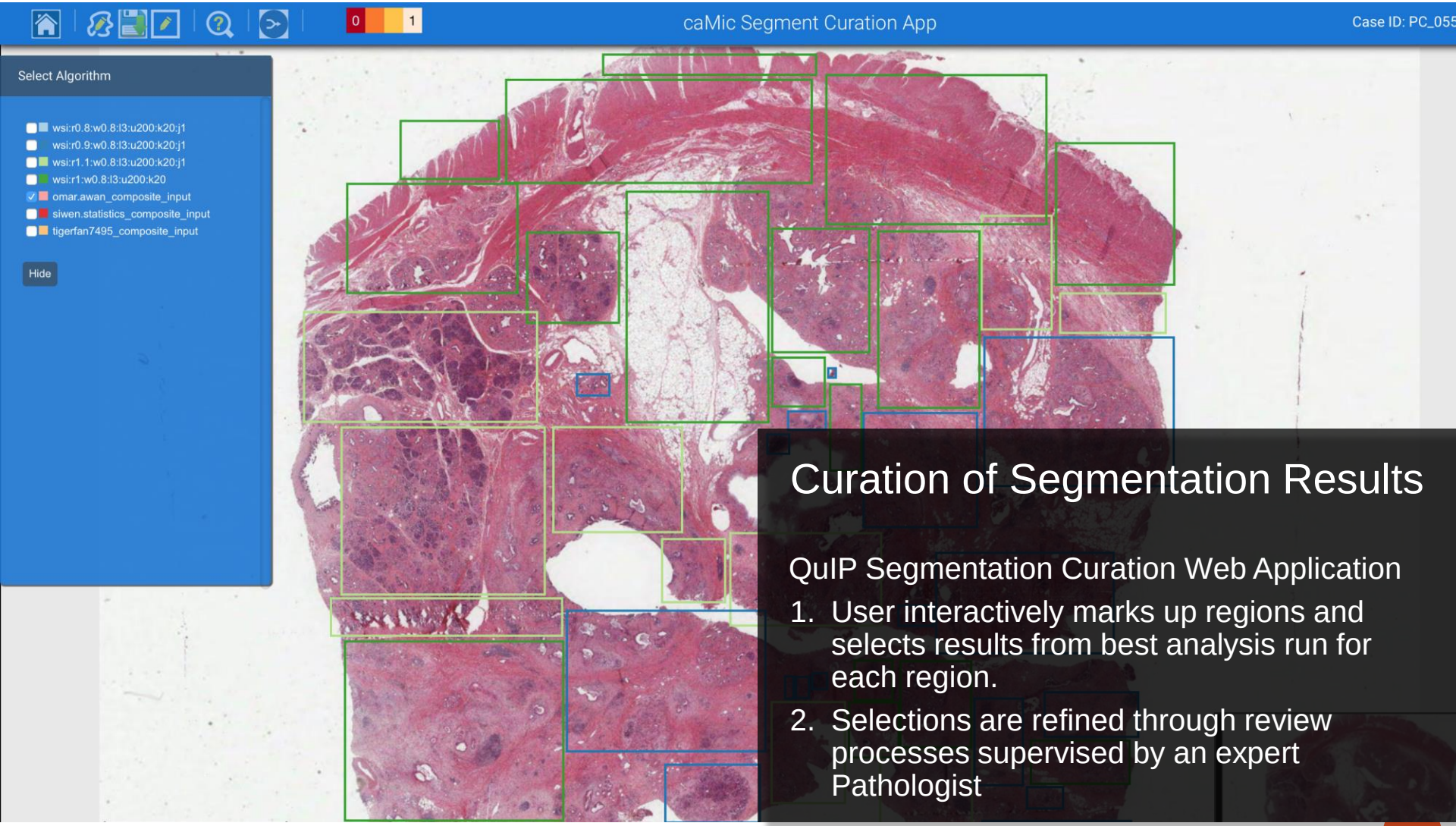
- Supplement registry abstracts with images AND quantitative features
  - Curate Images; Extract and Curate Features; and Web-based Visualization
- Data → Breast and Pancreas Cancer
  Five Registries
  Currently 122 images and 450M objects
- High quality feature curation, using QuIP algorithms and tools, on a representative subset of data
- All images and features accessible via caMicroscope

Built with QuIP (ITCR U24 PI: Saltz) and caMicroscope (CBIIT CTIIP PI: Sharma)

SEER VIRTUAL TISSUE REPOSITORY

Stony Brook University

- Create linked collection of de-identified clinical data and whole slide images
- Extract features from a sample set of images (pancreas and breast cancer).
- Enable search, analysis, epidemiological characterization
- Pilot focus on extreme outcome Breast Cancer, Pancreatic Cancer cases
- Display images and analyzed features



Curation of Segmentation Results

QuIP Segmentation Curation Web Application

1. User interactively marks up regions and selects results from best analysis run for each region.
2. Selections are refined through review processes supervised by an expert Pathologist

TIL quantitation and distribution

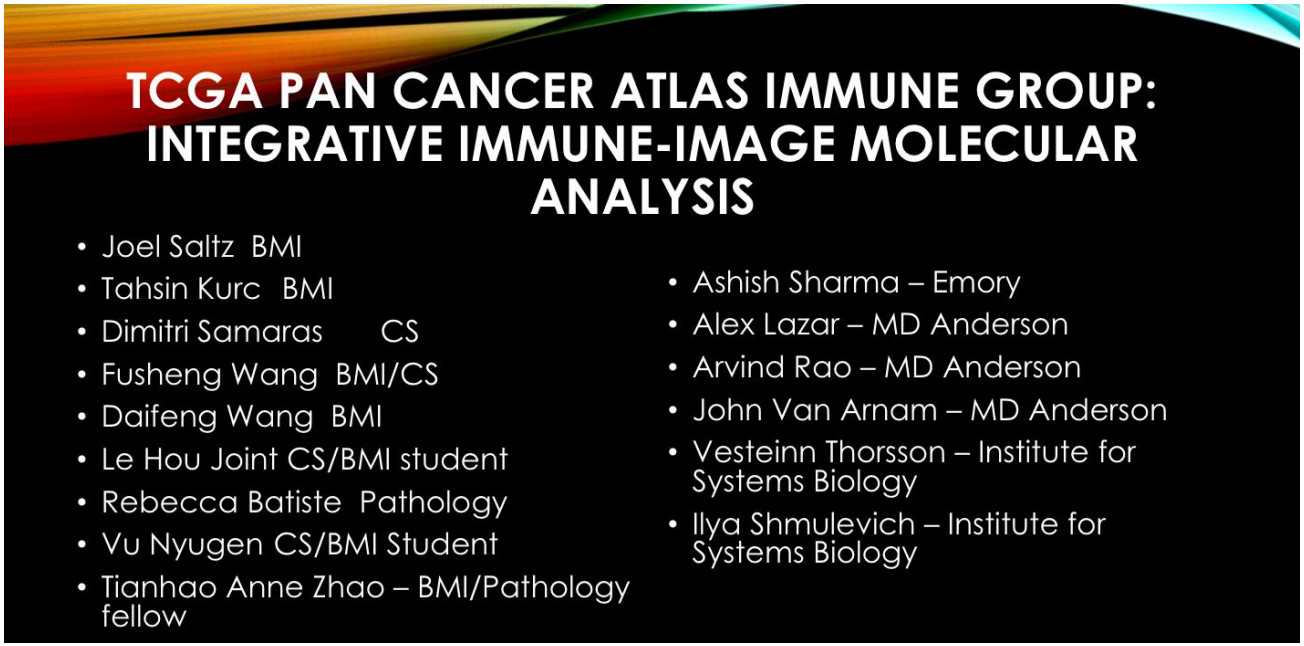
Stony Brook University

- The most common diagnostic tool in pathology is the H&E tissue image
- FDA just approved use of whole slide images in primary Pathology diagnosis
- TCGA dataset, which comprises 33 tumor types, contains over 30,000 tissue slide images.
- Link pattern of tumor infiltrating distribution to outcome, “omics”, treatment
- Deep Learning TIL method requires modest training and curation – suitable for high throughput analyses

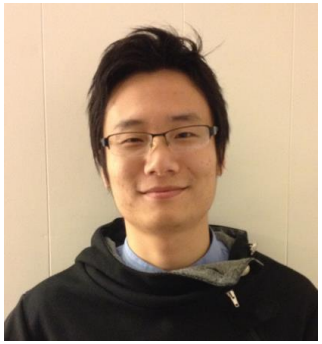
Importance of Immune System in Cancer Treatment and Prognosis

- Tumor spatial context and cellular heterogeneity are important in cancer prognosis
- Spatial TIL densities in different tumor regions have been shown to have high prognostic value – they may be superior to the standard TNM classification
- Immune related assays used to determine Checkpoint Inhibitor immune therapy in several cancer types
- Strong relationships with molecular measures of tumor immune response – results to soon appear in TCGA Pan Cancer Immune group publications
- TIL maps being computed for SEER Pathology studies and will be routinely computed for data contributed to TCIA archive
- Ongoing study to relate TIL patterns with immune gene expression groups and patient response

- Stony Brook, Institute for Systems Biology, MD Anderson, Emory group
- TCGA Pan Cancer Immune Group – led by ISB researchers
- Deep dive into linked molecular and image based characterization of cancer related immune response



Deep Learning and Lymphocytes: Stony Brook Digital Pathology Trainee Team



Le Hou – Graduate Student
Computer Science

Anne Zhao – Pathology Informatics
Biomedical Informatics, Pathology
(now Surg Path Fellow SBM)

Vu Nguyen– Graduate Student
Computer Science

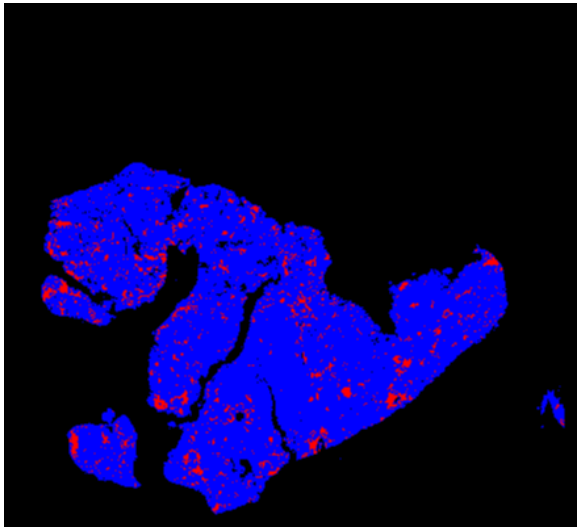
Raj Gupta – Pathology Informatics
Biomedical Informatics, Pathology

ATM | Annals of Translational Medicine

Ann Transl Med. 2016 Apr; 4(7): 142.
doi: 10.21037/atm.2016.03.28
PMCID: PMC48423

Importance of tumor infiltrating lymphocytes in non-small cell lung cancer?

Roy M. Bremnes,[1,2] Tom Donnem,[1,2] and Lill-Tove Busund[3,4]



Percentage 5-year disease specific survival rates according to TNM and Immunoscore

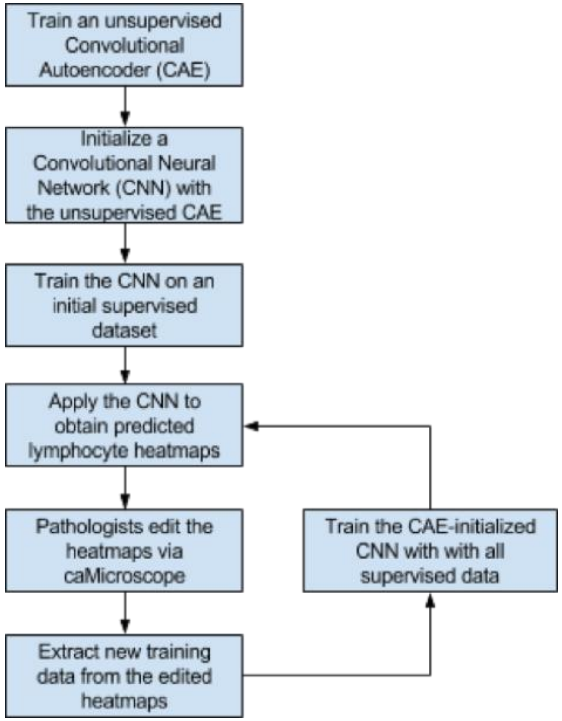
TNM-I		Immunoscore (stromal CD8)		
		Low	Intermediate	High
pStage	IA	71	75	87
	IB	59	73	83
	IIA	51	58	61
	IIB	25	55	61
	IIIA	18	41	68

5-year DSS rates
≤ 40 %
41–59 %
60–80 %
> 80 %

Deep Learning Training, Validation and Prediction

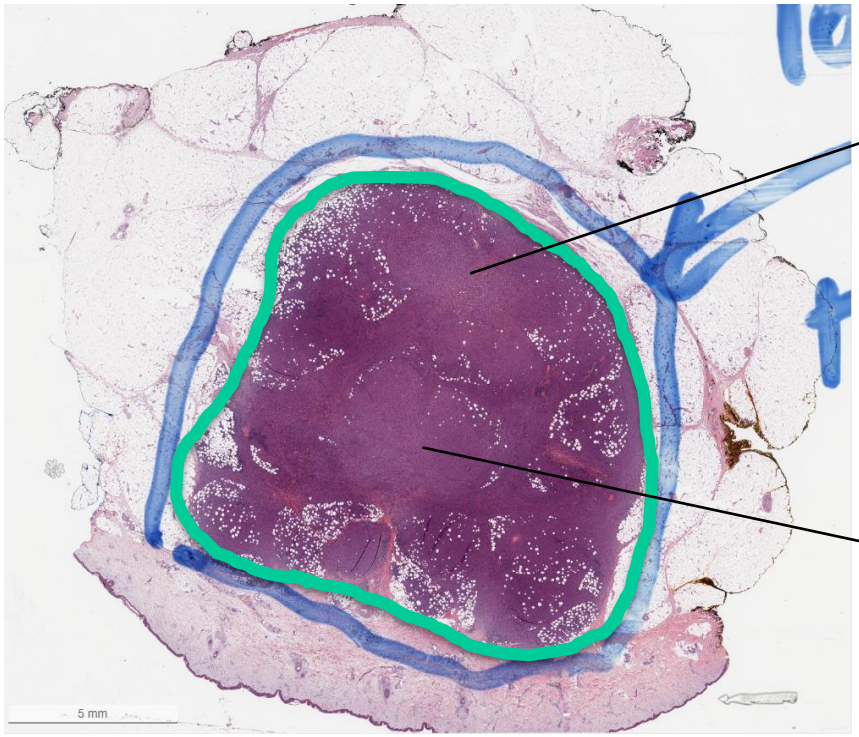
Stony Brook University

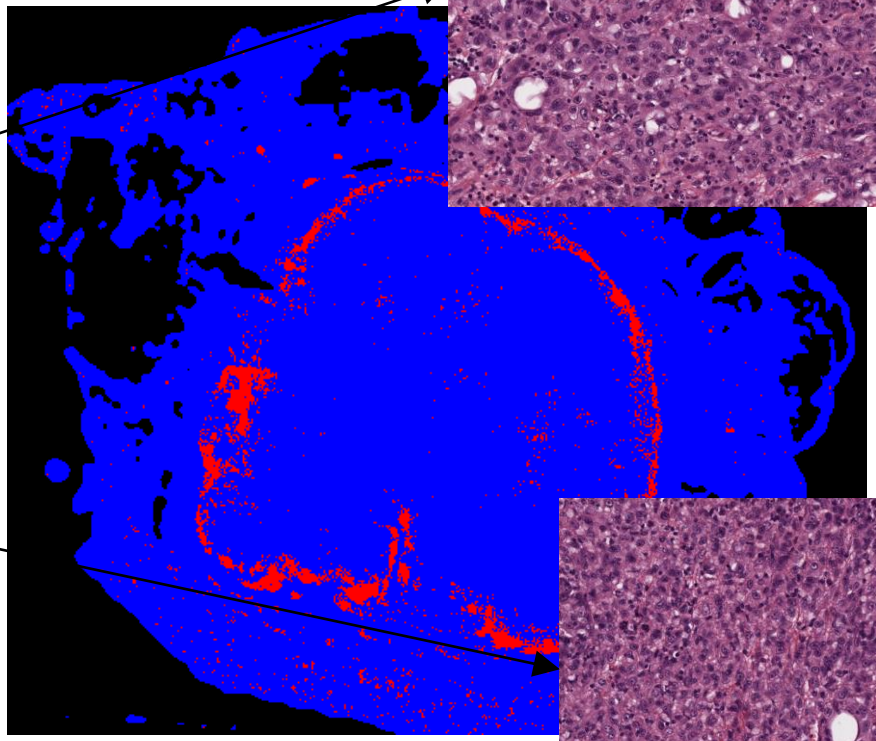
- Algorithm first trained on image patches
- Several cooperating deep learning algorithms generate heat maps
- Heat maps used to generate new predictions
- Companion molecular statistical data analysis pipelines

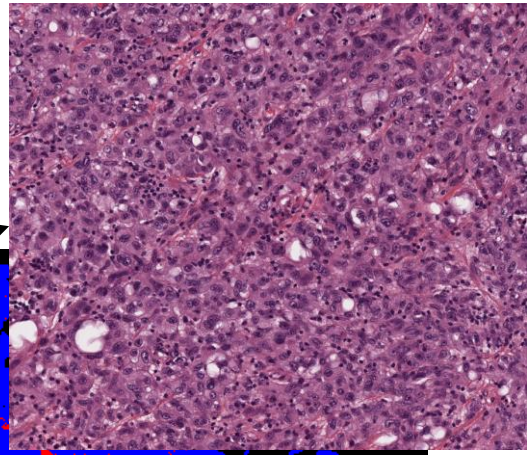


Tumor Infiltrating Lymphocyte Maps and Classification

Stony Brook University







Clustering and TIL Maps

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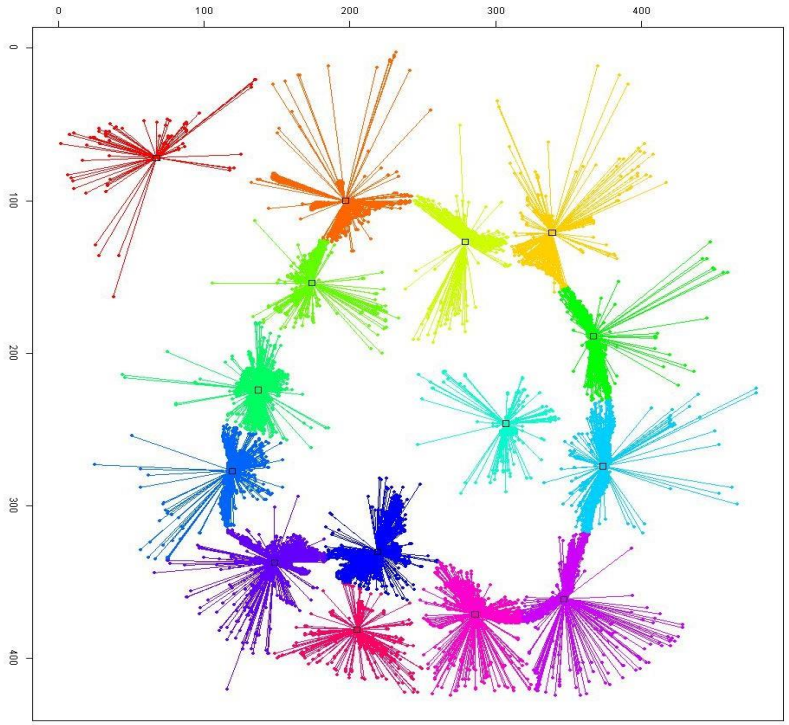
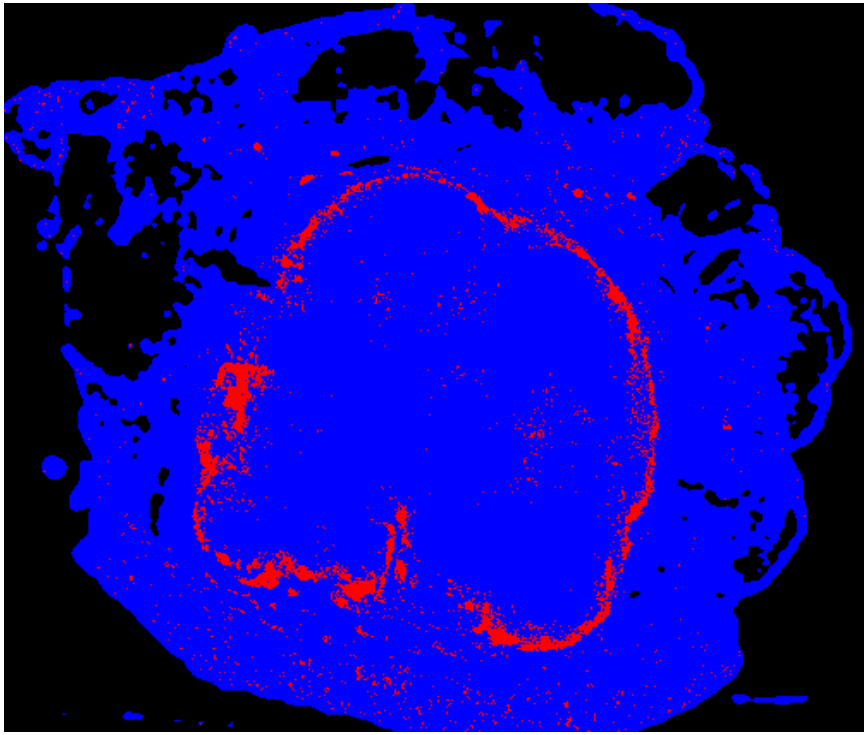


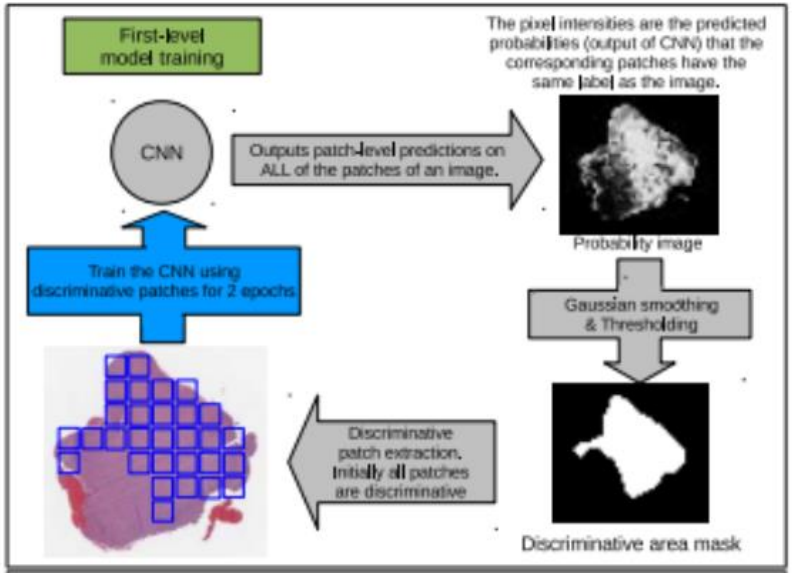


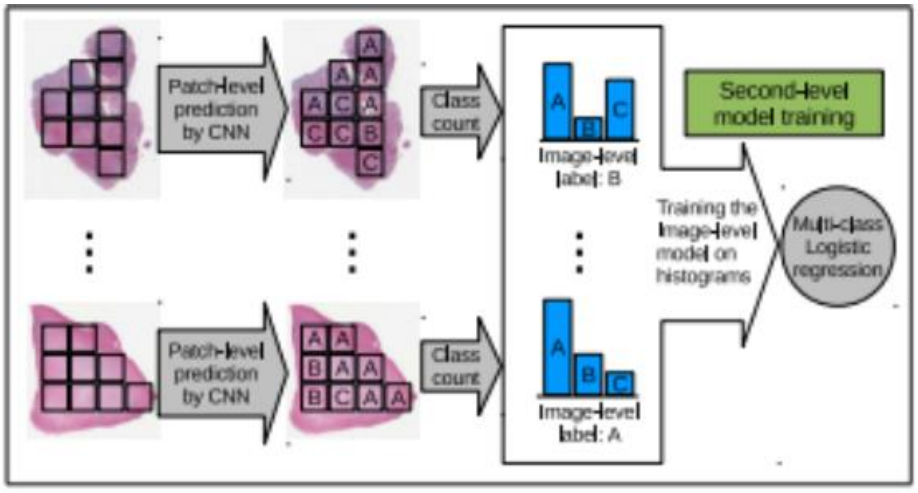
Tumor Classification – Reduce Inter-observer variability

Stony Brook University

Patch-Based Convolutional Neural Network for Whole Slide Tissue Image Classification

Le Hou, Dimitris Samaras, Tahsin M. Kurc, Yi Gao, James E. Davis, Joel H. Saltz; The IEEE Conference on Computer Vision and Pattern Recognition (CVPR), 2016, pp. 2424-2433





Tumor Classification Results

Stony Brook University

Glioma is
- The most common brain cancer
- The leading cause of cancer-related deaths in people under age 20

Methods	Accuracy
VGG16 features + BoW + SVM	0.667
Patch-CNN + Voting	0.710
Patch-CNN + Max-pooling	0.710
Our method	**0.771**
Pathologists' Agreement [M. Gupta 2015] (on a similar dataset)	0.7-0.8

Confusion Matrix: OA is very hard even for pathologists	GBM	OD	OA	DA	AA	AO
Glioblastoma, Grade IV (GBM)	214		2		1	
Oligodendroglioma, Grade II (OD)	1	47	22	2		1
Oligoastrocytoma, Grade II & III (OA)	1	18	40	8	3	1
Diffuse Astrocytoma, Grade II (DA)	3	9	6	20		1
Anaplastic Astrocytoma, Grade III (AA)	3	2	3	3	4	
Anaplastic Oligodendroglioma, Grade III (AO)	2	2	3			1

Le Hou, Dimitris Samaras, Tahsin Kurc, Yi Gao, Liz Vanner, James Davis, Joel Saltz

Information Technology for Cancer Research NCI Biomedical Informatics and Information Technology and NCI Cancer Imaging Program

Stony Brook University

- 8+ major projects encompassing Pathology Informatics – will hear about several in the next three days
- Broad recognition of importance of Radiology/Pathology/"omics" Integration
- Development of a Cancer Imaging Commons
- Peer institutions developing linked clinical/image sharing, feature extraction and trust fabric

Thanks!