

## Collaborative Medical Vision for Precision Medicine: The Quest for Interpretable and Explainable ML Models



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Imaging Informatics for Precision Medicine Lab



# Al-Informed Clinician

# Clinician-Informed AI

# Imperfect Data Scenarios where Clinician-AI collaboration is important

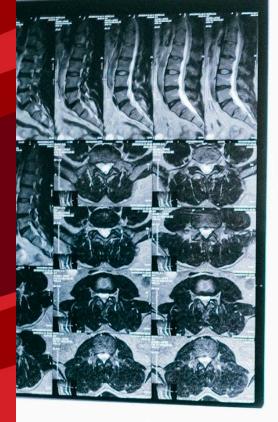
- □ Missing Modalities [MICCAI '23, ICCV '23]
- Costly Annotations [ICLR '23, ECCV '22, NeruIPS '23]
- Scarcity of datasets [MICCAI '23, IPMI '23]
- Unpaired data [CVPR '22]
- Complex Reasoning [CVPR '24, MeDIA'24]





## From purely data-driven models to...

## Data-informed and domain-inspired models

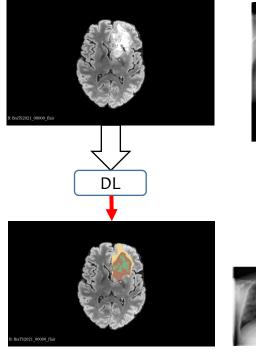


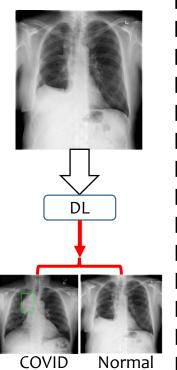


## Radiologist-in-the-Loop

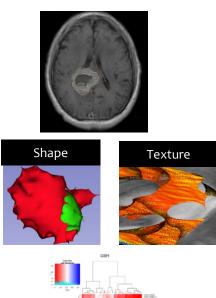
## Can Radiologists' Eye Gaze Information Augment ML decisions?

#### Deep Learning based Analysis





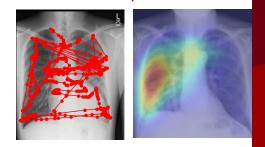
#### Radiomic Analysis



Tumor grading

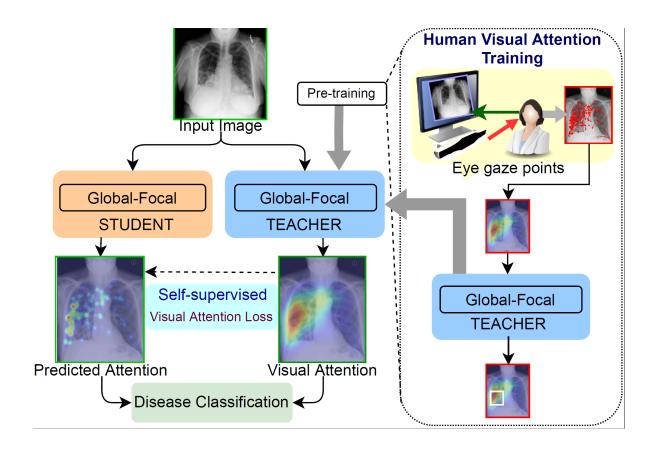
## Radiologist Eye-gaze maps





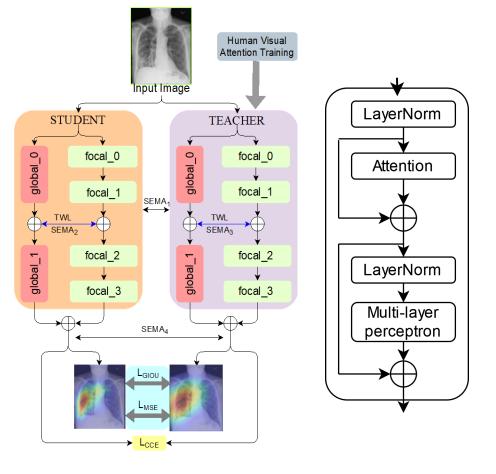
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RadioTransformer: A Cascaded Global-Focal Transformer for Visual Attention–guided Disease Classification





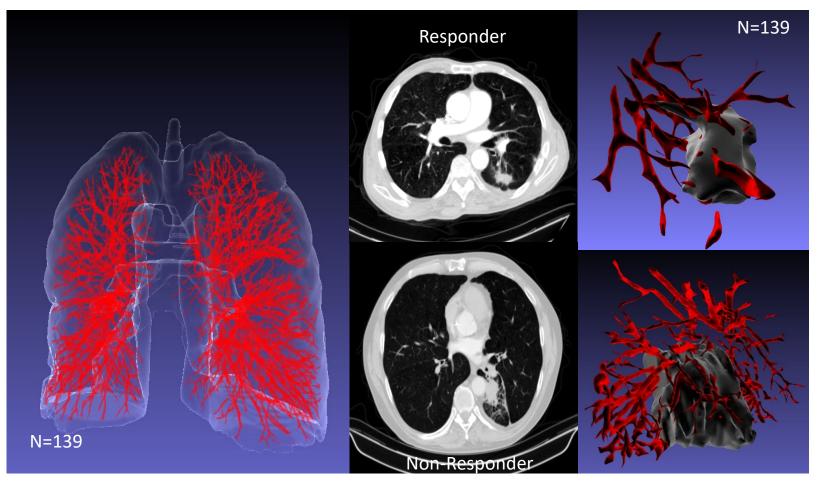
Bhattacharya et al, MICCAI 2022, ECCV 2022

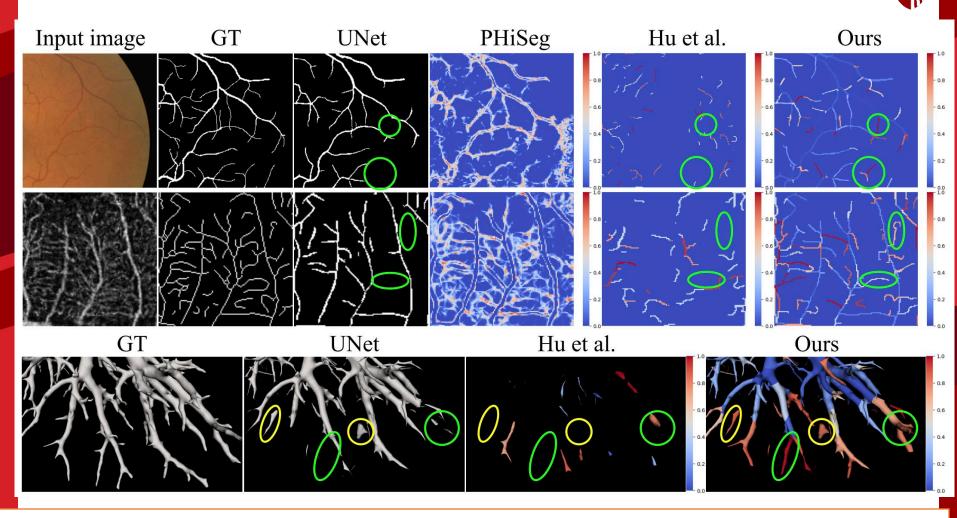


A <u>global-focal transformer architecture</u> to capture coarse-fine search behavior of radiologists.
Global module learns high-level coarse representations and the focal module learns low-level granular representations.

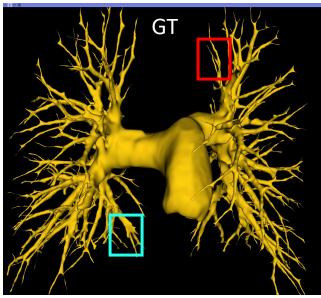
$Classification \rightarrow$	Pneumonia			COVID-19			14-Thoracic			COVID-19 (Test)						
$Dataset \rightarrow$	Cell	[33]	RSNA	A [ <mark>69</mark> ]	SIIM	[37]	Rad [	9,62]	NIH	[86]	VBD	) [ <mark>56</mark> ]	MIDRO	C [76, 77]	SBU [	11,67]
Architectures↓	F1	AUC	F1	AUC	F1	AUC	F1	AUC	F1	AUC	F1	AUC	F1	AUC	F1	AUC
R50 [18]	59.78	81.70	93.75	98.91	43.01	98.85	94.03	99.27	11.91	74.04	21.76	95.86	23.04	96.32	15.11	65.16
R101 [18]	71.93	83.64	94.84	99.21	39.22	96.98	85.36	97.62	11.20	73.30	32.77	96.24	22.31	93.87	24.22	99.20
R152 [18]	74.30	87.49	91.97	98.57	43.04	98.18	70.21	87.90	10.67	71.37	32.42	96.58	19.22	83.09	24.58	99.61
R50v2 [19]	78.96	87.32	96.60	99.44	47.99	99.79	92.82	99.06	11.42	73.11	34.11	96.32	23.93	98.72	18.71	78.27
R101v2 [19]	52.11	71.23	96.39	99.33	45.83	99.26	97.46	99.82	11.99	73.46	32.18	96.55	04.86	42.13	19.43	82.47
R152v2 [19]	53.44	71.97	95.30	99.01	47.10	99.71	97.76	99.82	11.93	73.23	32.69	96.54	23.07	95.89	23.03	96.25
D121 [20]	70.05	81.97	96.25	99.34	47.59	99.82	95.72	99.51	13.81	78.83	28.71	96.01	24.88	99.82	20.67	88.35
D169 [20]	59.18	76.56	88.86	95.60	46.40	99.68	94.33	99.52	15.21	79.90	32.90	96.46	24.97	99.84	20.13	85.95
D201 [20]	71.93	82.98	95.43	99.04	48.17	99.83	97.81	99.85	14.84	81.38	34.66	96.41	24.99	99.99	21.08	89.53
ViT-B16 [12]	73.85	83.40	76.35	86.06	36.22	95.74	88.25	98.42	05.50	82.06	34.80	95.69	08.47	42.15	11.49	50.22
ViT-B32 [12]	70.02	76.41	79.11	90.74	30.42	92.12	86.73	98.09	06.51	83.77	30.57	94.58	17.50	76.52	18.26	77.75
ViT-L16 [12]	69.59	83.31	85.41	94.53	34.16	95.75	90.11	98.70	08.16	81.60	33.99	95.40	11.17	47.79	15.54	62.72
ViT-L32 [12]	76.38	87.07	69.32	88.86	28.45	92.54	88.40	98.35	06.35	84.96	33.24	95.36	10.21	47.35	03.92	30.82
CCT [17]	62.10	71.18	80.60	92.04	32.63	95.33	92.52	99.11	08.08	85.37	30.25	95.12	23.98	98.53	19.43	83.21
Swin0 [44]	66.04	83.74	96.27	99.57	47.63	99.66	97.53	99.92	07.90	74.62	34.30	95.08	13.74	63.07	17.77	75.47
Swin1 [44]	73.74	86.91	96.65	99.58	47.30	99.56	94.94	99.64	08.30	74.18	34.27	95.13	15.47	69.00	17.64	73.68
RadT w/o (HVAT+VAL)	79.56	89.82	97.85	99.78	48.42	99.69	98.13	99.94	05.97	85.48	37.64	96.83	16.70	71.78	22.19	93.75
RadT	77.40	88.80	98.75	99.85	48.74	99.65	99.39	99.98	04.21	85.43	37.32	96.84	18.17	79.60	22.18	94.76

## Immunotherapy Response Prediction

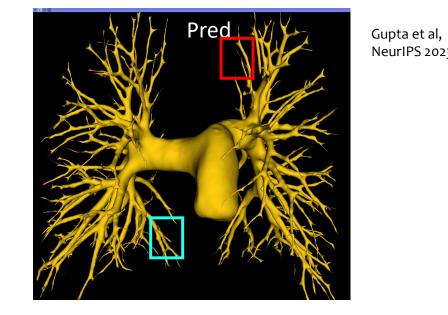




How do we use uncertainty estimation to efficiently obtain high fidelity segmentations?

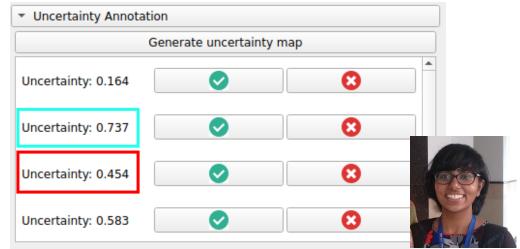






NeurIPS 2023

#### Uncertainty estimation-driven interactive segmentation

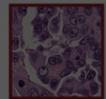


# Pathologist-in-the-Loop

#### Interpretability in Computational Pathology: From Black-box to Glass-box







Intracellular musin droplets Nuclear atypia and prominent nucleoli

Nuclear atypia and prominent nucleoli

Identifying salient regions in a WSI

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- Several MIL methods provides the visualization of attention maps from the learned patch-level attention.
- Though useful, they may not offer an automated understanding of the model's prediction due to a lack of user-friendly feature grounding.
- Also these visualizations are hard and subjective for experts to interpret.





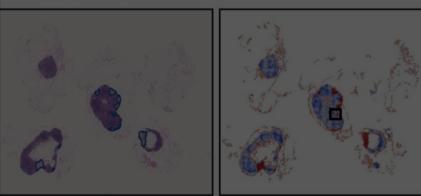
Keratinization and

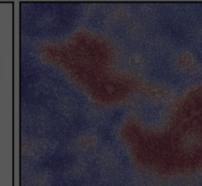
intracellular bridges

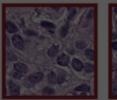




Nuclear atypia.







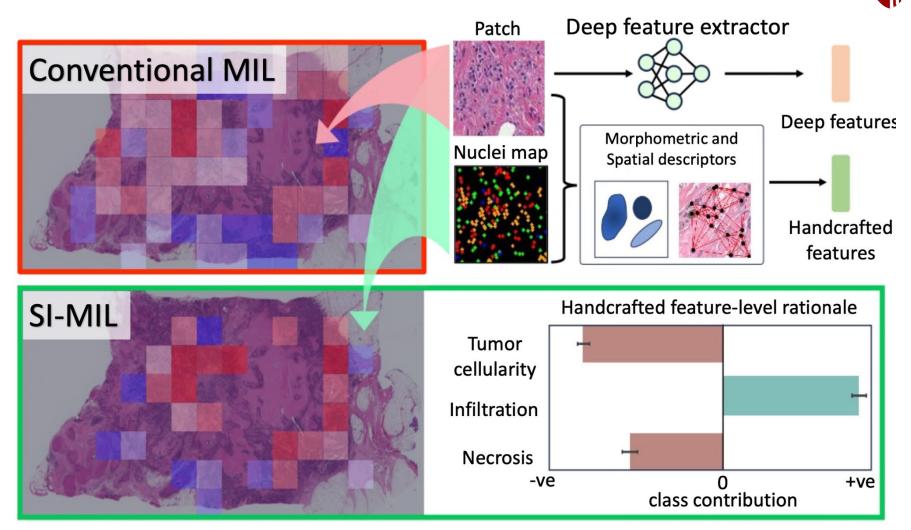




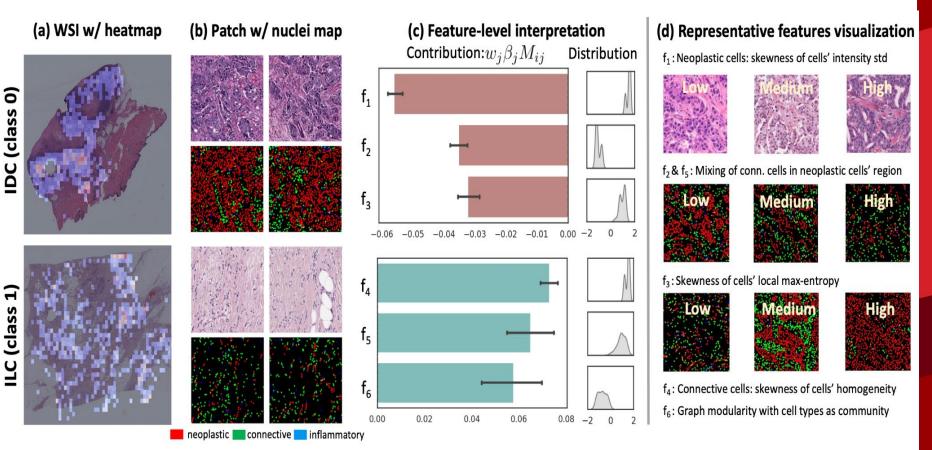
Larger epithelioid cells with nuclear irregularity and increased cytoplasm in a background of small lymphocytes



#### Whole slide image classification

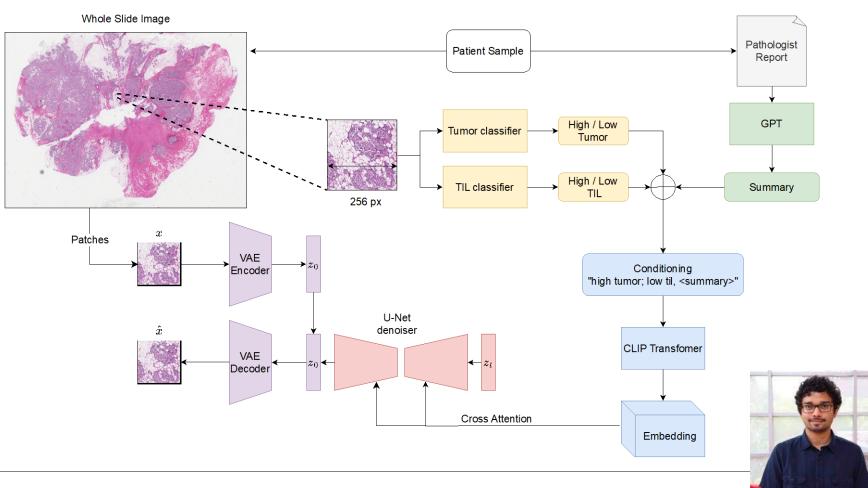


#### **Proposed method – Self Interpretable Models**





## Text-conditioned image generation



#### User

Extract information from breast pathology report. List the histological classification, i.e. type of cancer or DCIS, subtype, description of any necrosis, any mention of tumor infiltrating lymphocytes, histological grade, nuclear grade, lymphovascular invasion, calcification, receptor status, IHC and any other ancillary testing results. List out and expand the main points.

#### The report is

Subtype LumA, Path No.: Date Obtained: (Age: Date Received: F. See Addendum/Procedure. SPECIMEN: A:Lymph node, left axilla sentinel, biopsy. B:Breast, left, modified radical mastectomy. DIAGNOSIS(ES): A. Lymph node, left axilla sentinel, biopsy: .... Metastatic carcinoma, following carcinoma of breast. B. Breast, left, modified radical mastectomy:...

#### GPT

The breast pathology report indicates the following information:

1. Histological classification: The patient has Luminal A subtype breast cancer. The biopsy of the left axilla sentinel lymph node shows metastatic carcinoma following breast carcinoma.

2. Subtype: The invasive carcinoma is of the lobular type, poorly differentiated and multifocal, with extensive lymphatic permeation. Lobular neoplasia, type B (pleomorphic), is widespread. The report also mentions fibrocystic disease, proliferative, with atypia.

3. Necrosis: No mention of necrosis.

4. Tumor infiltrating lymphocytes: The report mentions extensive lymphatic permeation but does not mention tumor infiltrating lymphocytes.

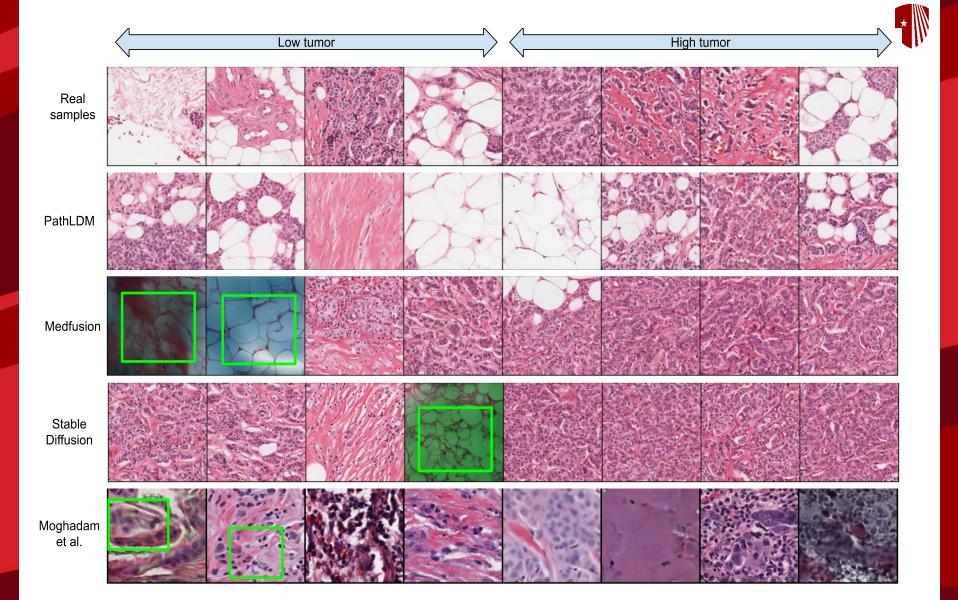
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#### User

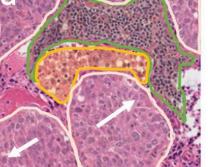
Please generate a succinct report in 75 words from the above information. Exclude any filler words or sentences. If something is not mentioned or specified, exclude it from the report. Low verbosity.

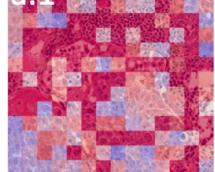
GPT

Report: Luminal A subtype breast cancer with metastatic carcinoma in axillary lymph nodes. Invasive carcinoma is of lobular type, poorly differentiated and multifocal, with extensive lymphatic permeation. Pleomorphic lobular neoplasia type B and cystic disease found. Nuclear grade 3, positive estrogen receptor and progesterone receptor expression with no Her-2/neu overexpression. Lymphovascular invasion present in lymphatics. No necrosis or tumor infiltrating lymphocytes mentioned.



# TCGA-LUN



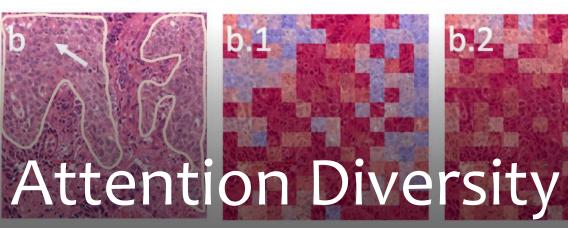




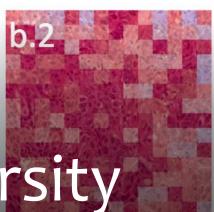


WO.







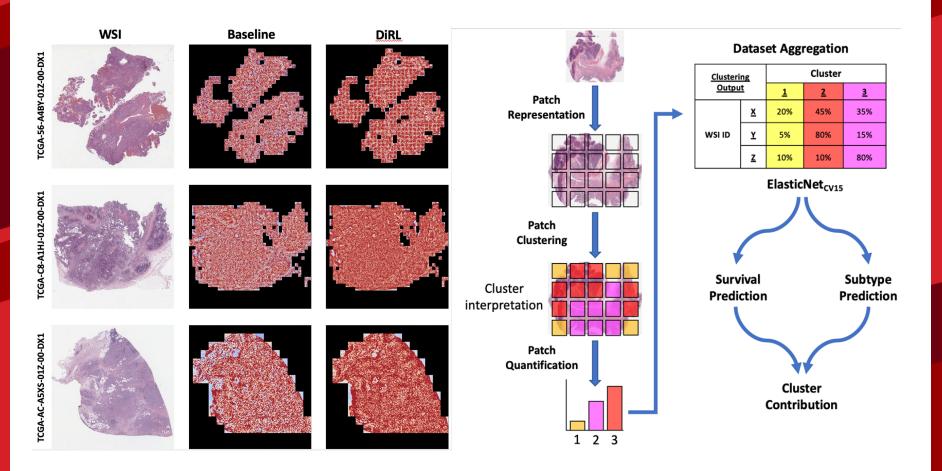




Matters!

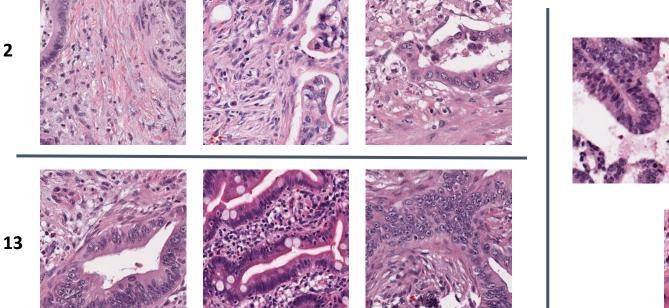
Kapse et al. MedIA, 2024





## **Pancreatic cancer - Basal**

Cluster	HR Beta	Subtype Beta	Description (Raj)	Parsed Description		
2	0.14	0.71	Stroma+Tumor	TME, Stroma+Tumor		
13	0.11	0.29	Normal+Tumor	TME, Stroma+Tumor		
4	0.07	0.25	Small dark nuclei	Small round black nuc		

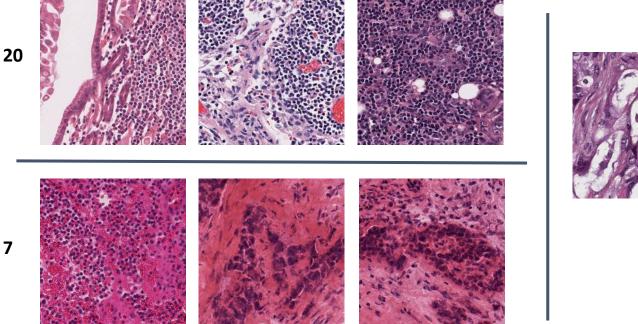


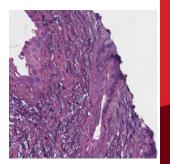
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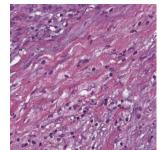
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### **Pancreatic cancer - Classical**

9	)	0.06	-0.92	Desmoplastic stroma +/- tumor, n	TME, Stroma+Tumor	
7	7	-0.03	-1.4	Bright pink	Bright pink, wavey	
2	0	0.27	-2.93	Lymph	Lymph Invasion	







#### **ACKNOWLEDGEMENTS**



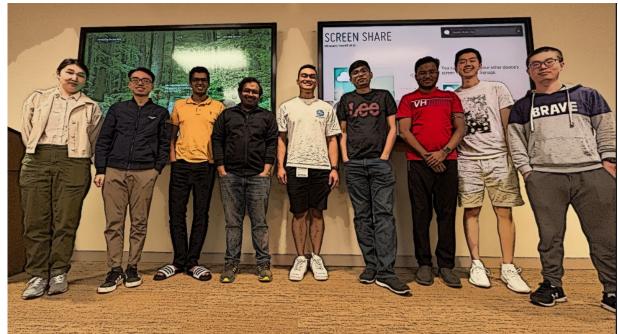
RUTGERS

Robert Wood Johnson Medical School















Stony Brook Medicine

## Thank you

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