August 22, 2024

Aly Khan Nuruddin

Expression-Based Molecular Subtyping & Classification of Bladder Cancer TCGA Data

Artificial Intelligence in Medicine (AIM) Lab

A Consensus Molecular Classification of Muscle-Invasive Bladder Cancer (MIBC)

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European Association of Urology (EAU).

Overview

Bladder Cancer:

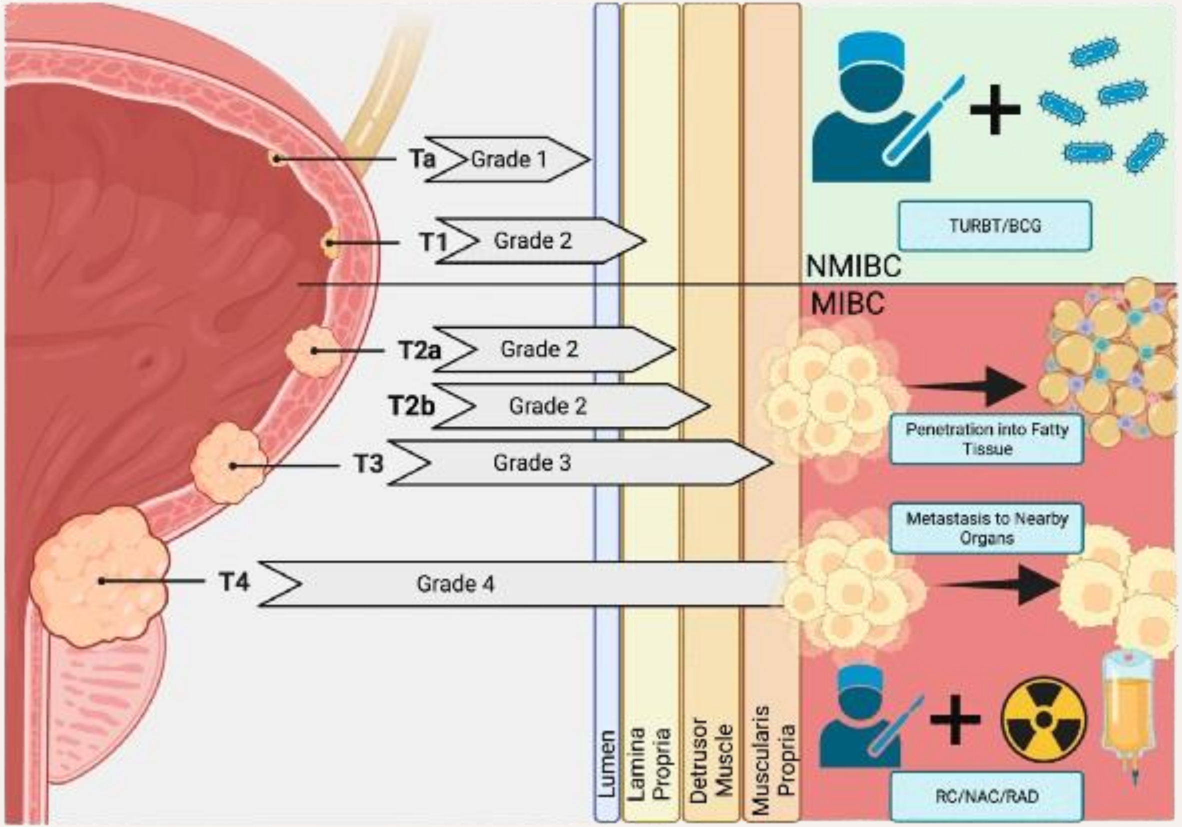
Urothelial Carcinoma Originating in Tissues of the Urinary System

Non-Muscle Invasive Bladder Cancer

Superficial Cancer Confined to Mucosa Layer

Muscle-Invasive Bladder Cancer

Aggressive Cancer Penetrating Muscle Layer



https://www.mdpi.com/2227-9059/11/2/539

Introduction

Existing Classification Systems:

Diversity of Molecular Subtypes Impedes Clinical Application

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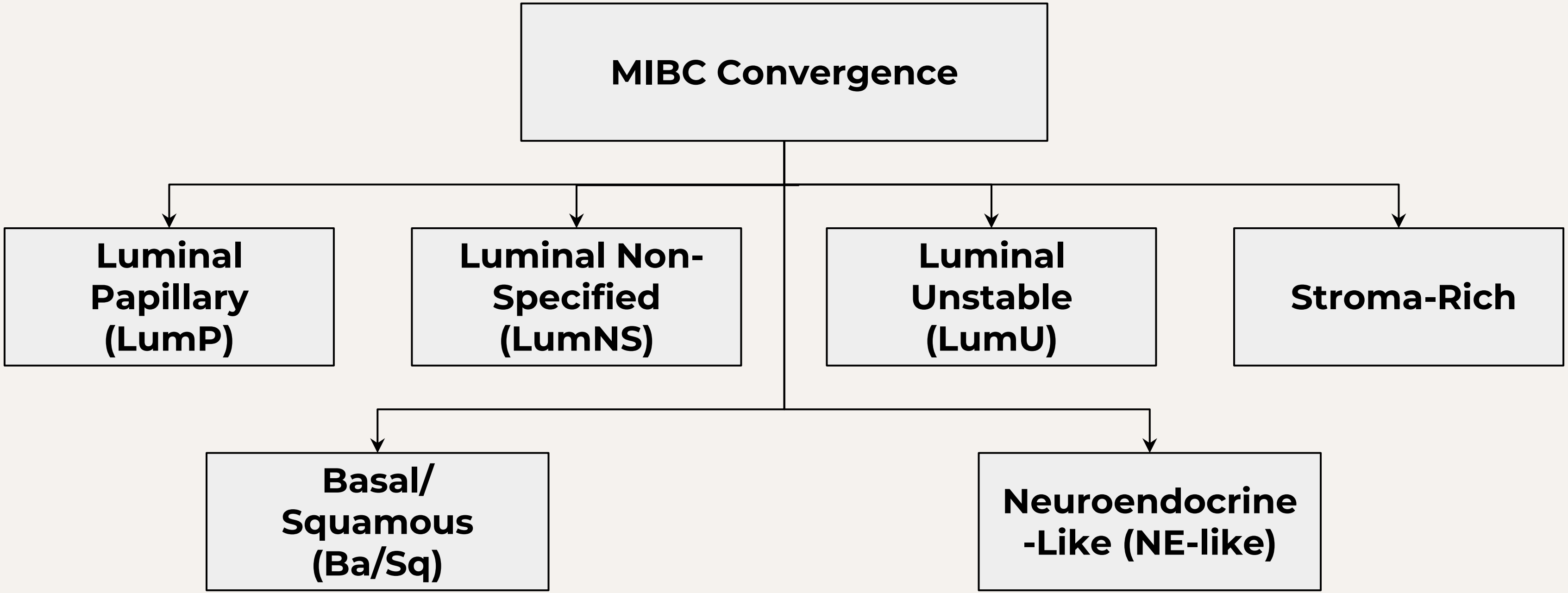
Lack of Naming Convention + Data Variability

Research Objective:

“Achieve International Consensus of MIBC Molecular Subtypes that Reconciles Published Classification Schemes”

Consensus Classification

Implementation: Nearest-Centroid Transcriptomic Classifier in R



Analytical Workflow

Patch Extraction

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Feature Extraction

⇩

Multiple Instance Learning (MIL)

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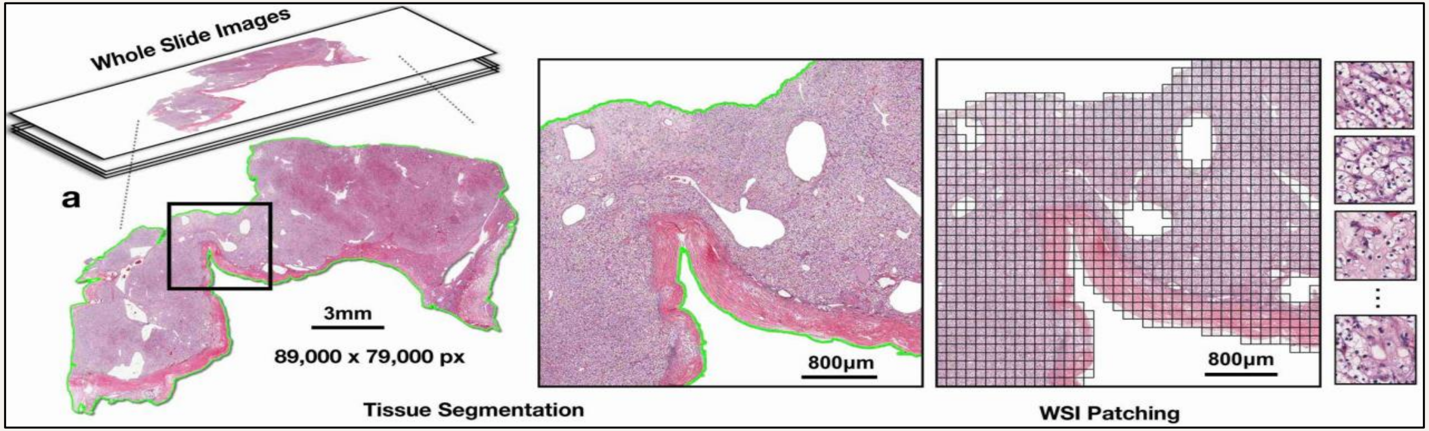
Information Visualization

Patch Extraction

Purpose: Facilitate Localized Deep Learning

Input: Masks Pre-Selected from HistoQC

Output: 1,500 Patches Per Whole Slide Image



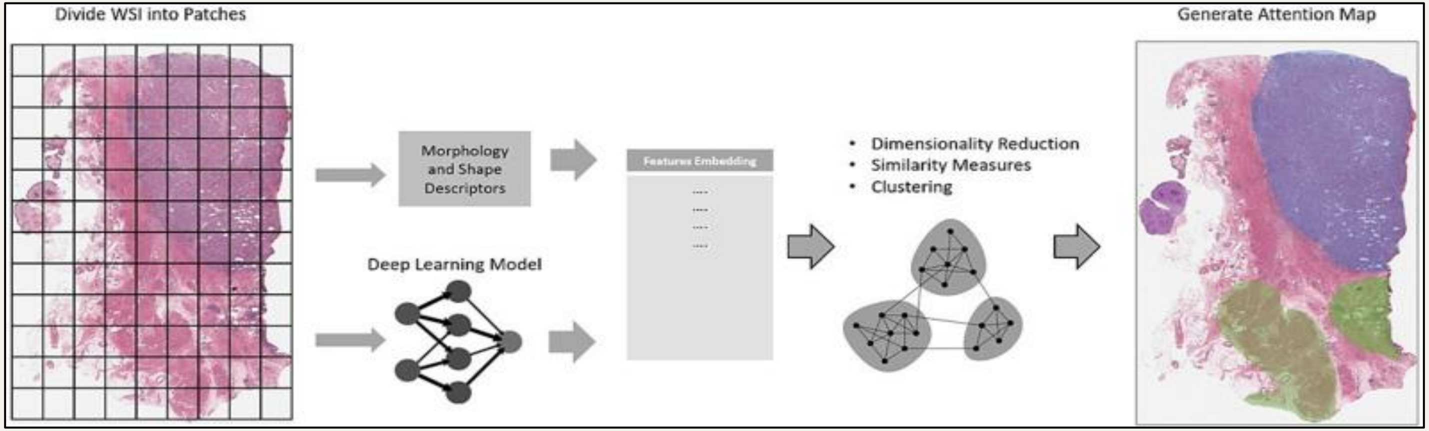
https://pixelscientia.com/articles/from-patches-to-slides/

Feature Extraction

Purpose: Meaningfully Represent Tissue Characteristics

Input: 1,500 Patches Per Whole Slide Image

Output: 458 Diagnostic + 463 Frozen .h5 Files



https://www.sciencedirect.com/science/article/pii/S215335392300149

Feature Encoders

CTransPath • Pre-Trained Vision Transformer for Unsupervised Contrastive Learning	**Lunit Dino** • Pre-Trained Vision Transformer for Self-Supervised Learning
Phikon • Pre-Trained Vision Transformer for Self-Supervised Learning	**PLIP** • Pre-Trained Vision Transformer for Pathology Image Retrieval
UNI • Pre-Trained Vision Transformer for Self-Supervised Learning	**vit** • Pre-Trained Vision Transformer for Self-Supervised Learning

Multiple Instance Learning

Purpose: Analyse Extracted Features at Bag-Level

Input: 458 Diagnostic + 463 Frozen .h5 Files for 20x Mag

Output: 90 Checkpoint + Output .pt Files per Model

Models:

1. DeepMIL
2. TransMIL
3. ClamSB

Data Folds:

1. Fold #1
2. Fold #2
3. Fold #3

Relevant Metrics:

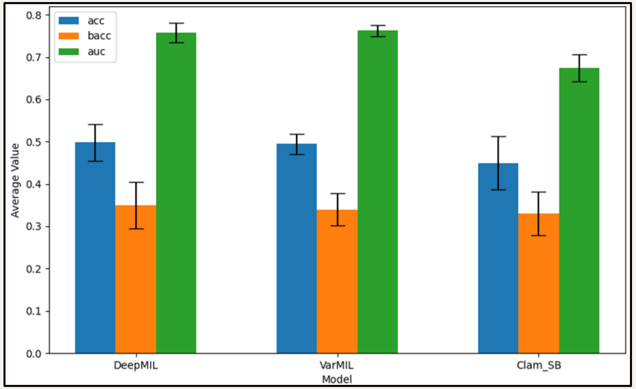
1. Accuracy
2. Bal. Accuracy
3. AUC

Others:

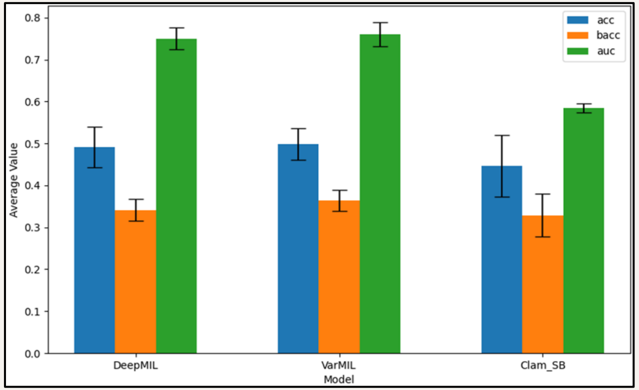
1. Time
2. Recall
3. Precision
4. F1-Score

DIAGNOSTIC

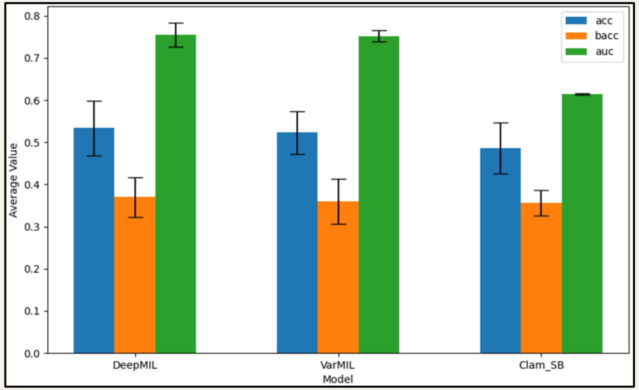
CTransPath



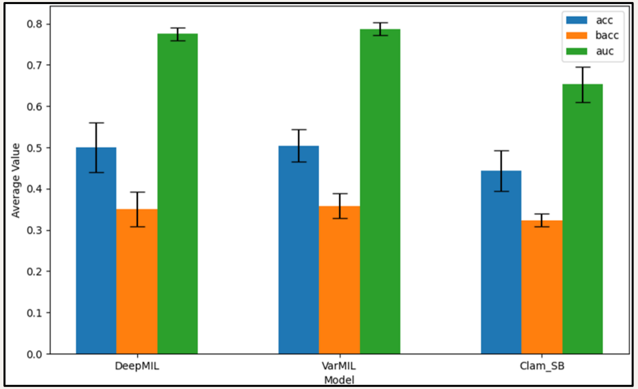
Phikon



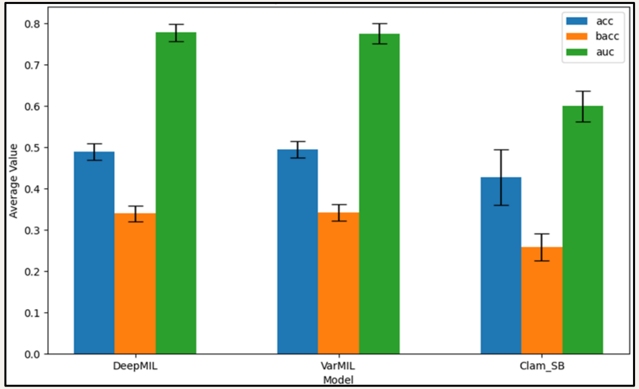
UNI



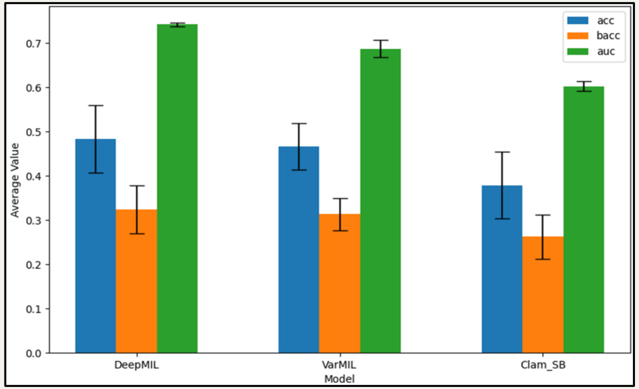
Lunit-Dino



PLIP

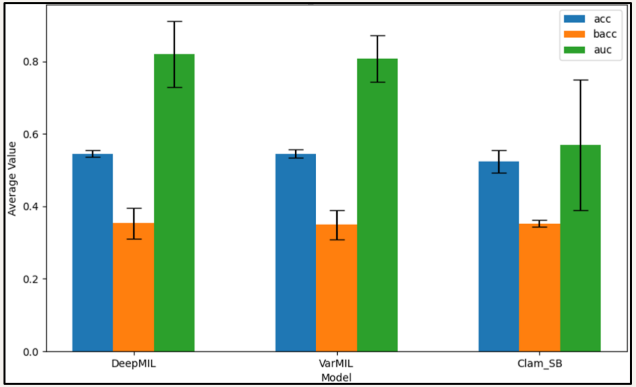


vit



FROZEN

CTransPat



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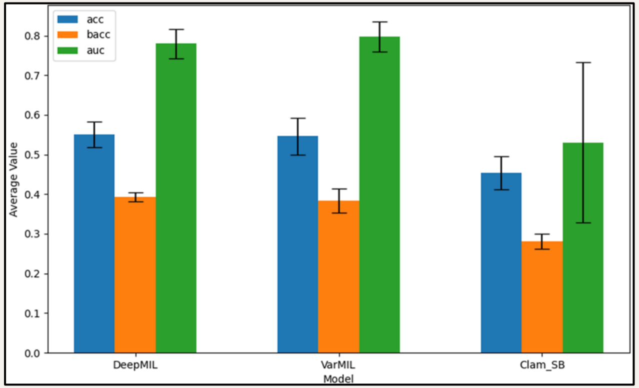

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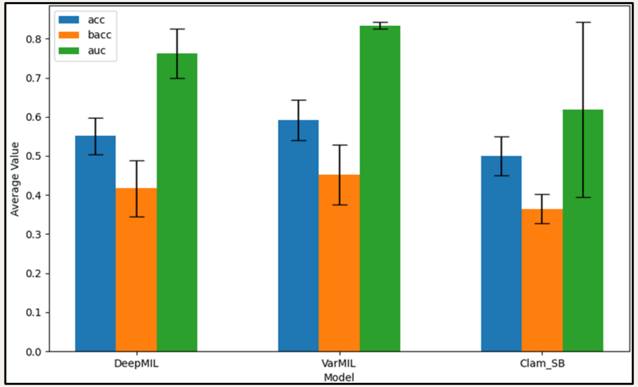

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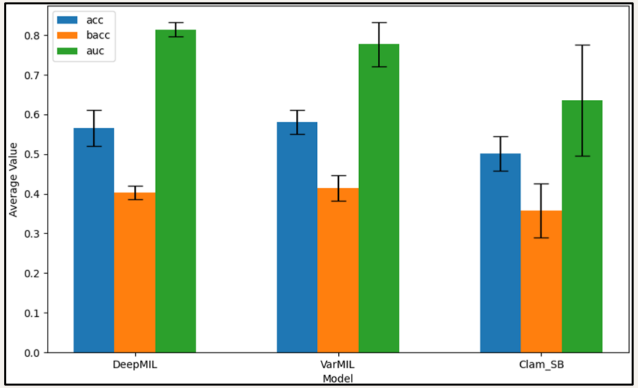

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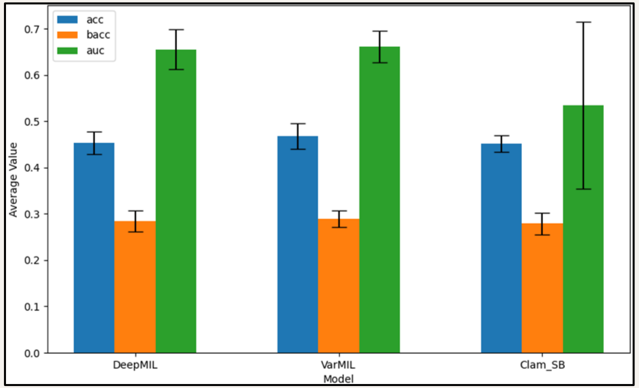

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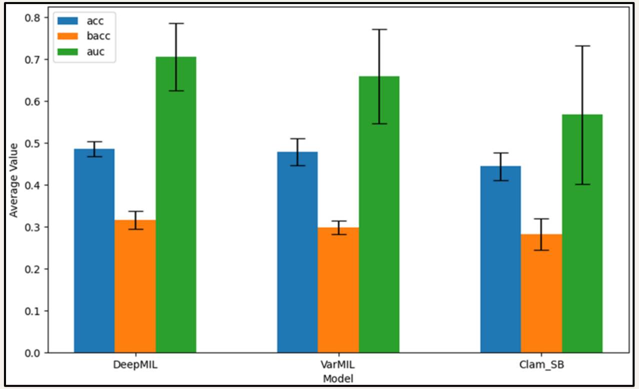


Summary of Findings

Observations:

- CTransPath, Phikon and UNI were the Highest Performing Encoders
- DeepMIL and VarMIL Consistently Provided the Highest Metrics
- AUC Varied the Most Between Models while BACC Varied the Least

Future Work:

- Implement Hyperparameter Tuning (Learning Rate, Weight Decay etc.)
- Experiment with Multi-Headed Attention Mechanisms or Hybrid Variants
- Use Cross-Validation to Prevent Over-Fitting and Increase Robustness

Information Visualization

Purpose: Determine Relationships Between Subtypes

Input: 458 Diagnostic + 463 Frozen .h5 Files for 20x Mag., Manifest File (patient_id, slide_id, subtype, slide_path)

Output: UMAP Plots

Slide-Level

Mean Pooling of 1,500 Patches + Filtering of Features with No Subtypes

Eg: (1,500, 768) → (1, 768)

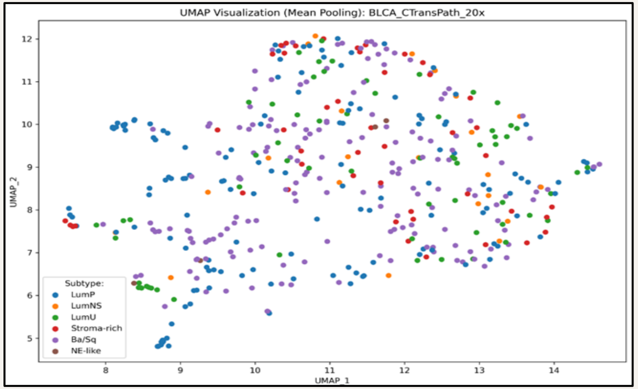
Patch-Level

Random Selection of 150 Patches + Filtering of Features with No Subtypes

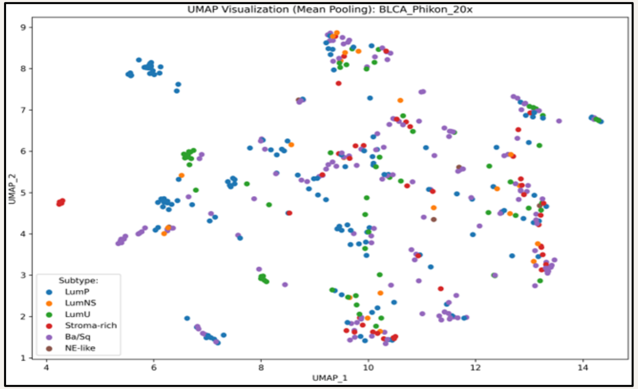
Eg: (1,500, 768) → (150, 768)

DIAGNOSTIC (Slide-Level)

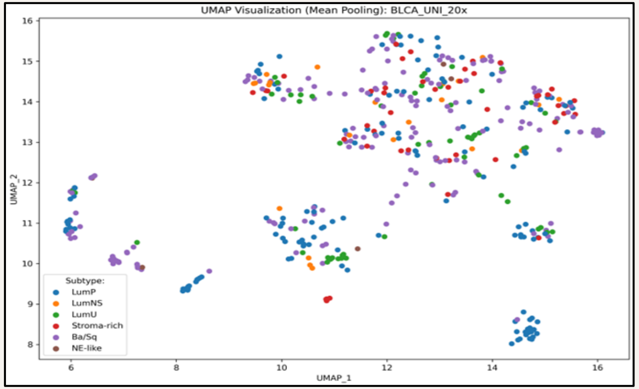
CTransPath



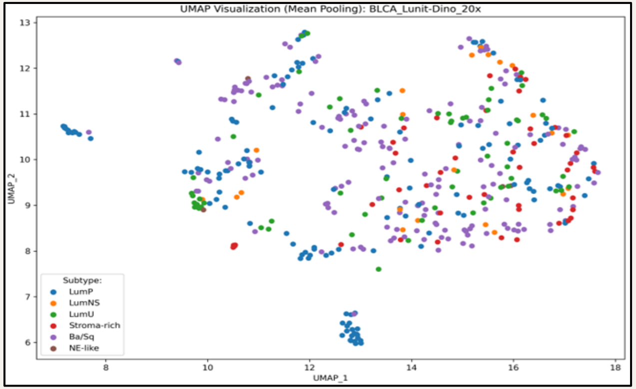
Phikon



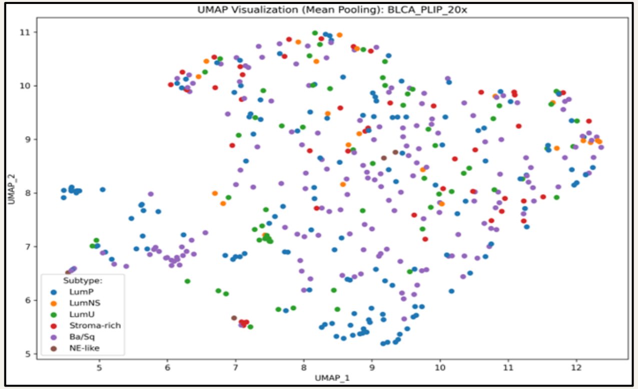
UNI



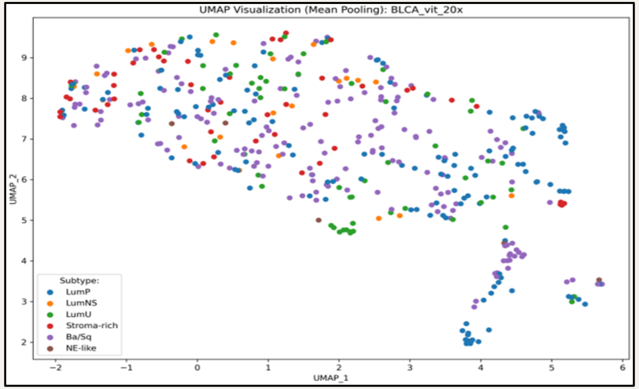
Lunit-Dino



PLIP

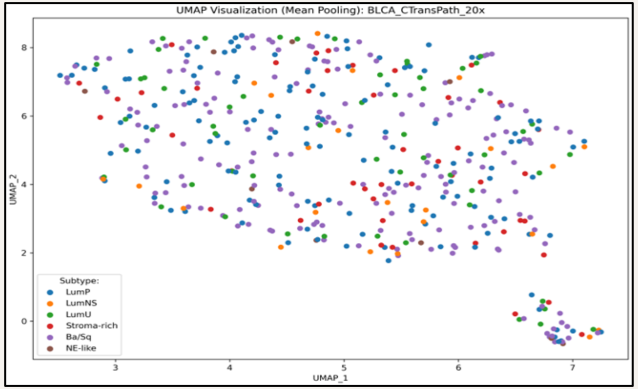


vit

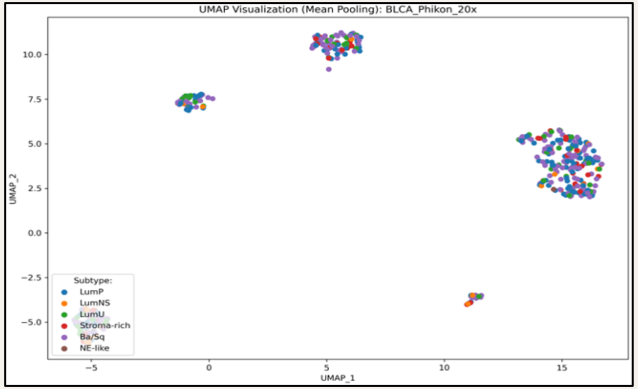


Frozen (Slide-Level)

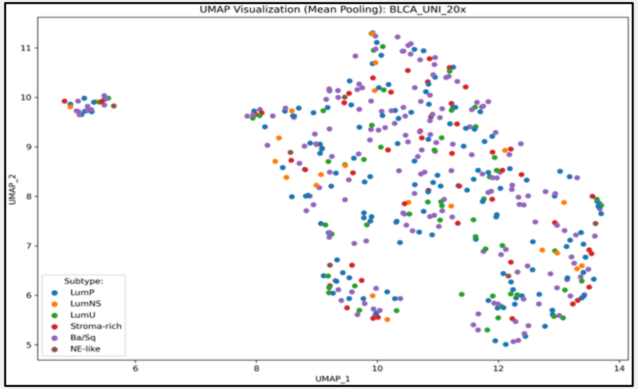
CTransPath



Phikon



UNI



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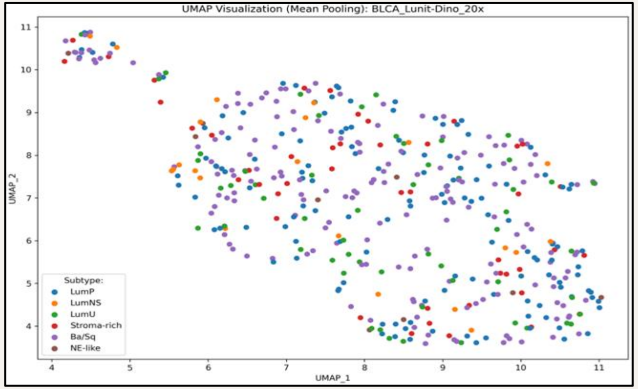

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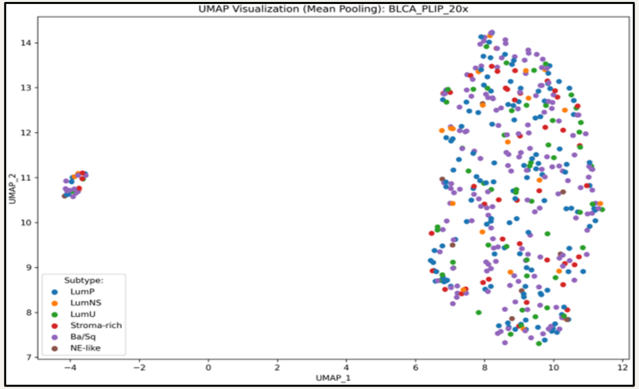

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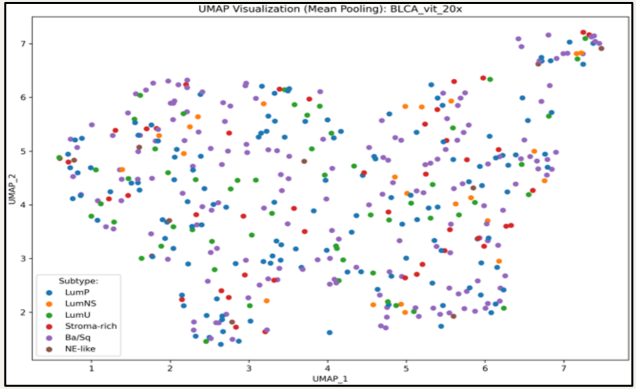
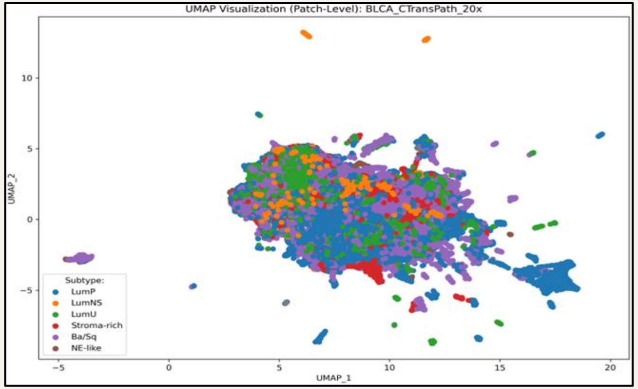


DIAGNOSTIC (Patch-Level)

CTransPath



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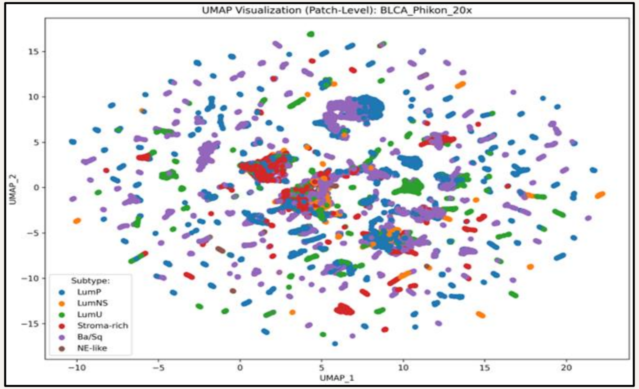

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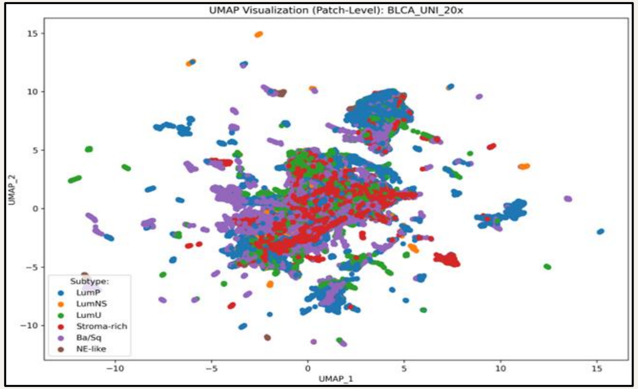

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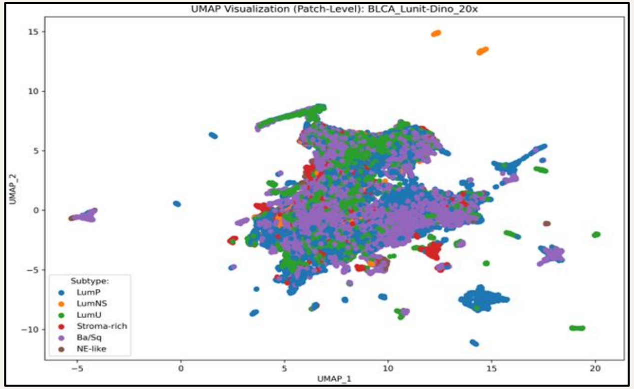
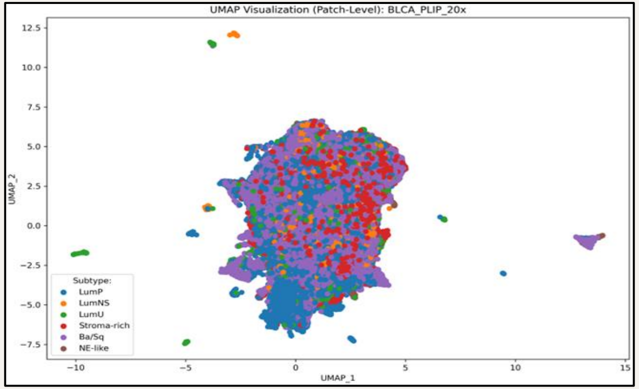
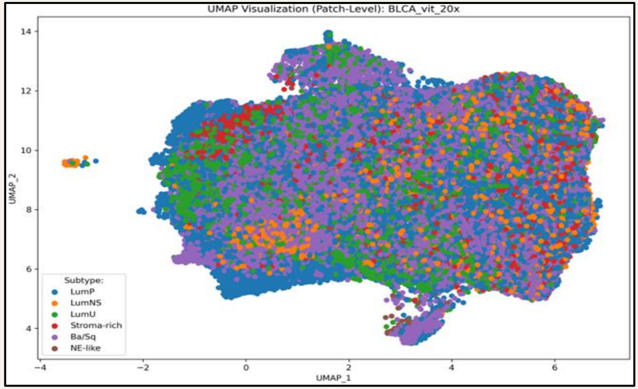


PLIP

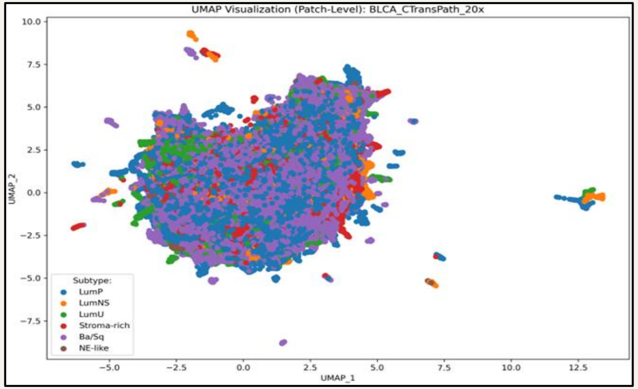


vit

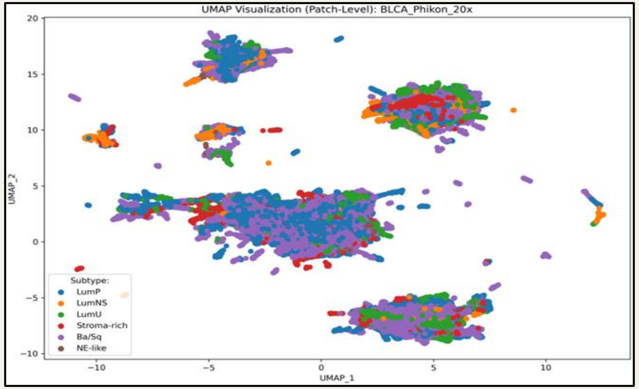


FROZEN (Patch-Level)

CTransPath



Phikon



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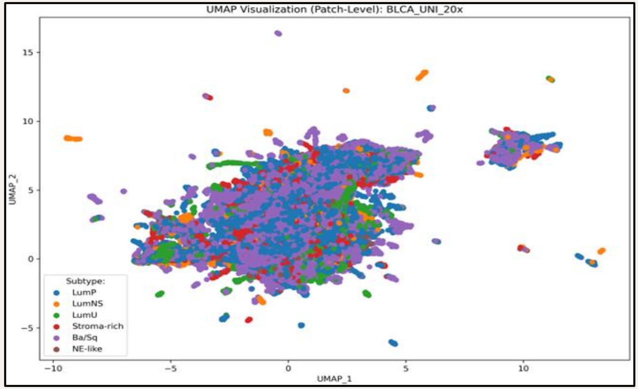

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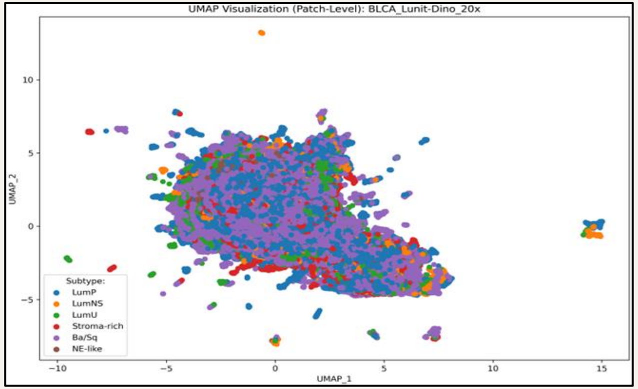

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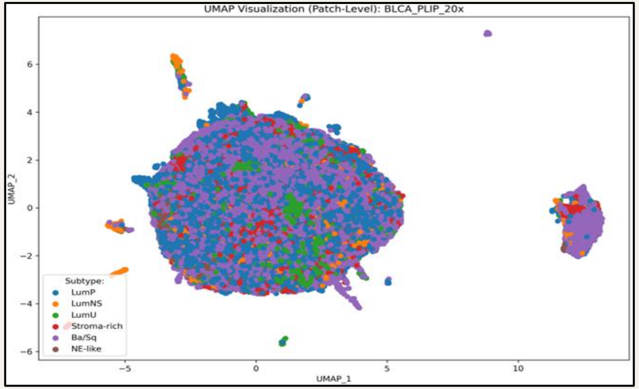

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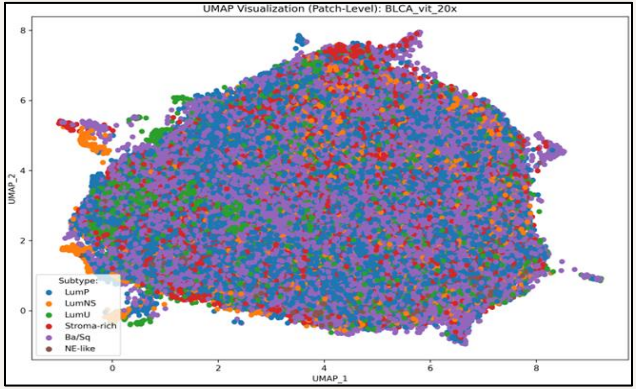

Summary of Findings

Observations:

- Patch-Level UMAPs Provided Higher Granularity than Slide-Level UMAPs
- Patch-Level UMAPs Capture Data Diversity Better than Slide-Level UMAPs
- Patch-Level UMAPs Retain Local Patterns Better than Slide-Level UMAPs

Future Work:

- Stratified Sampling Based on Patches of Interest + Extract More Samples
- Implement Weighted Aggression or Hierarchical Pooling at Slide-Level
- Perform Dimensionality Reduction (PCA, t-SNE) Prior to UMAP Plotting

Acknowledgements

Questions?