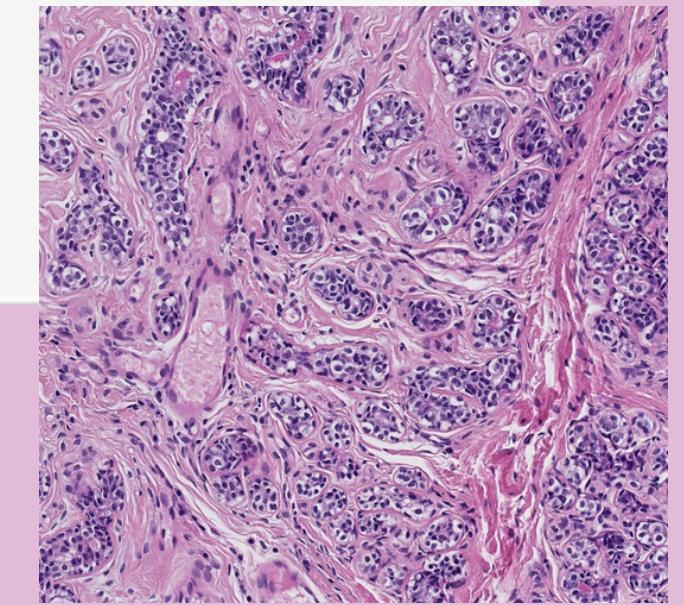


TiGER

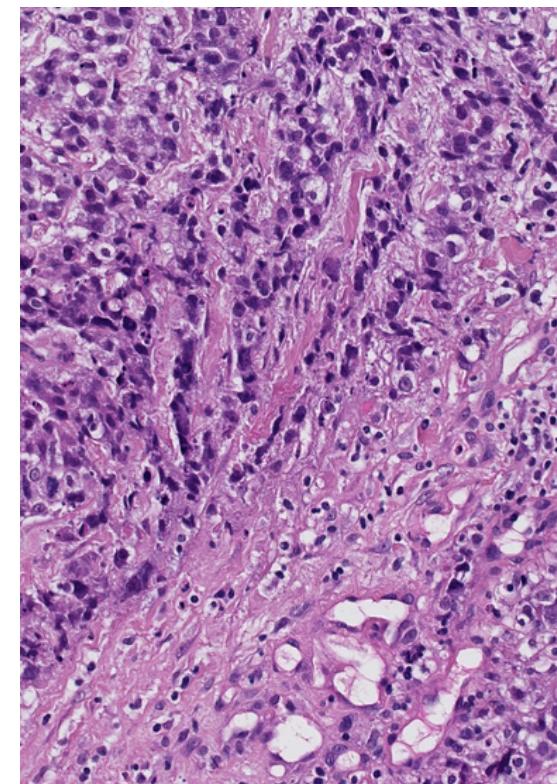
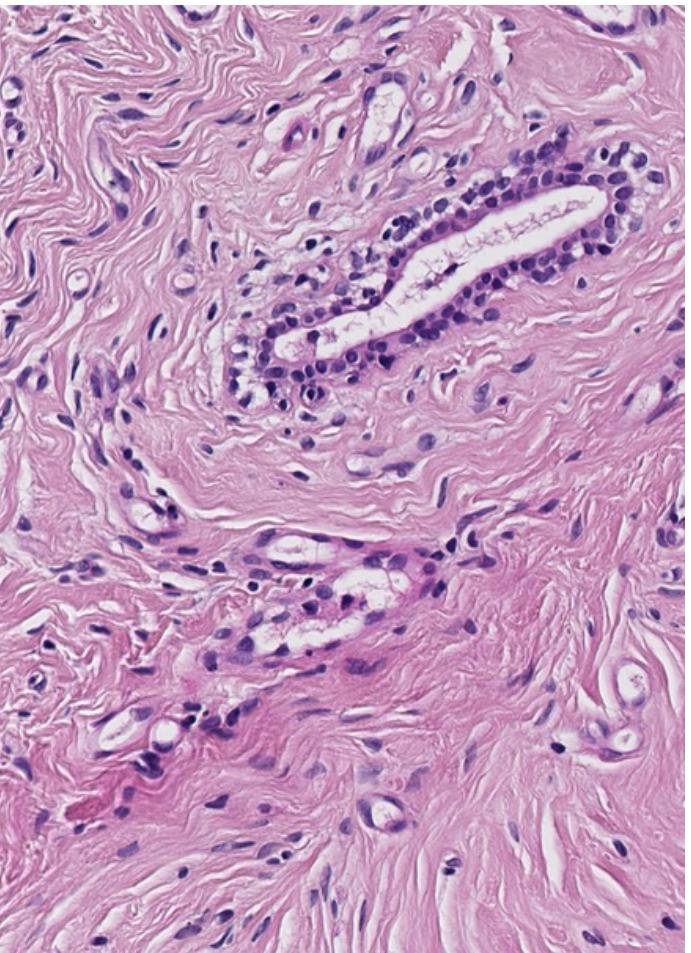
Tumor Infiltratin**G** lymphocytes in breast canc**ER**



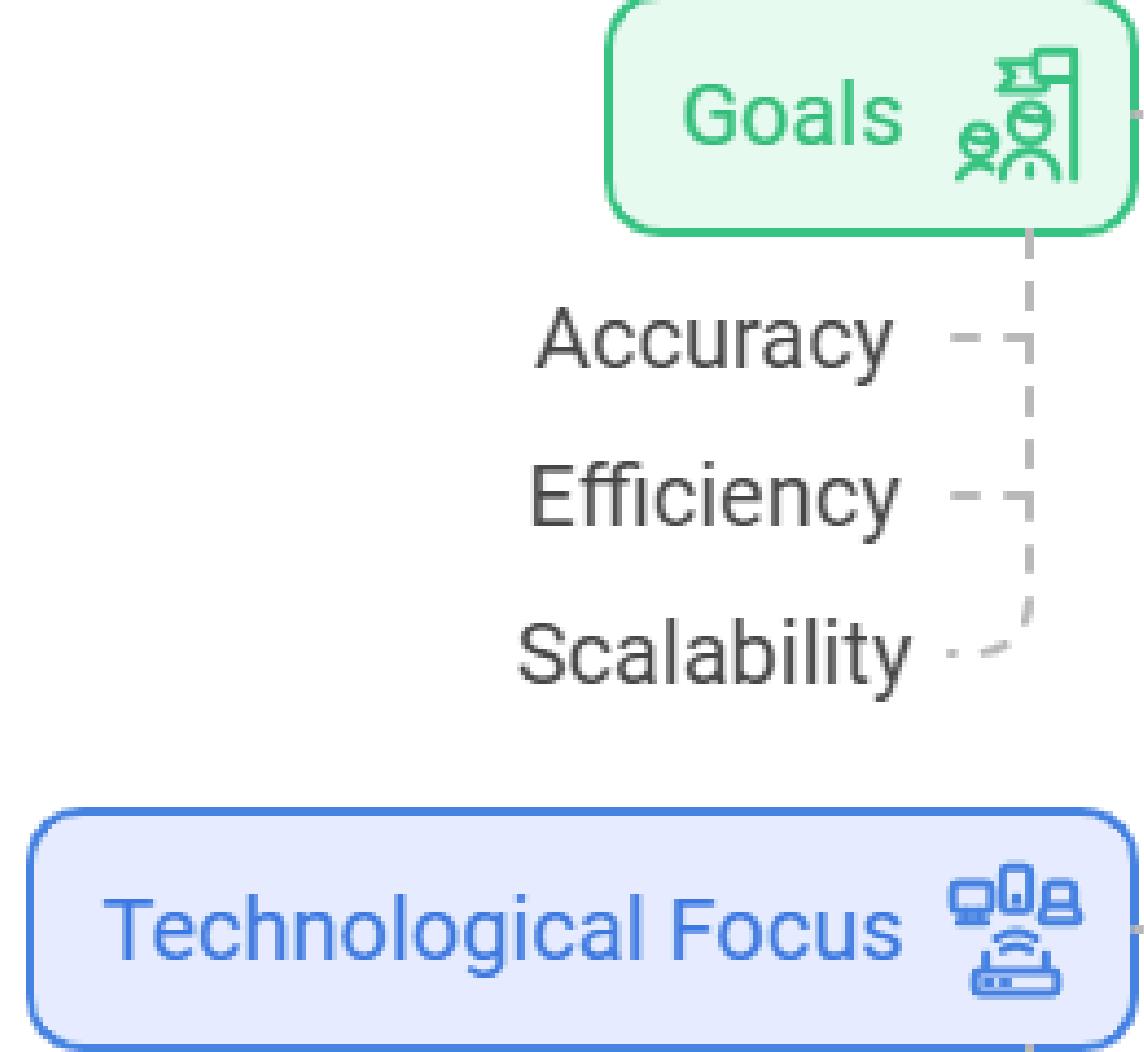
TIGER GRAND CHALLENGE

Automated Assessment of Tumor-Infiltrating Lymphocytes (TILs) in Breast Cancer

The TIGER Grand Challenge is an initiative aimed at advancing computational pathology through automated assessment of TILs in breast cancer histopathology slides.



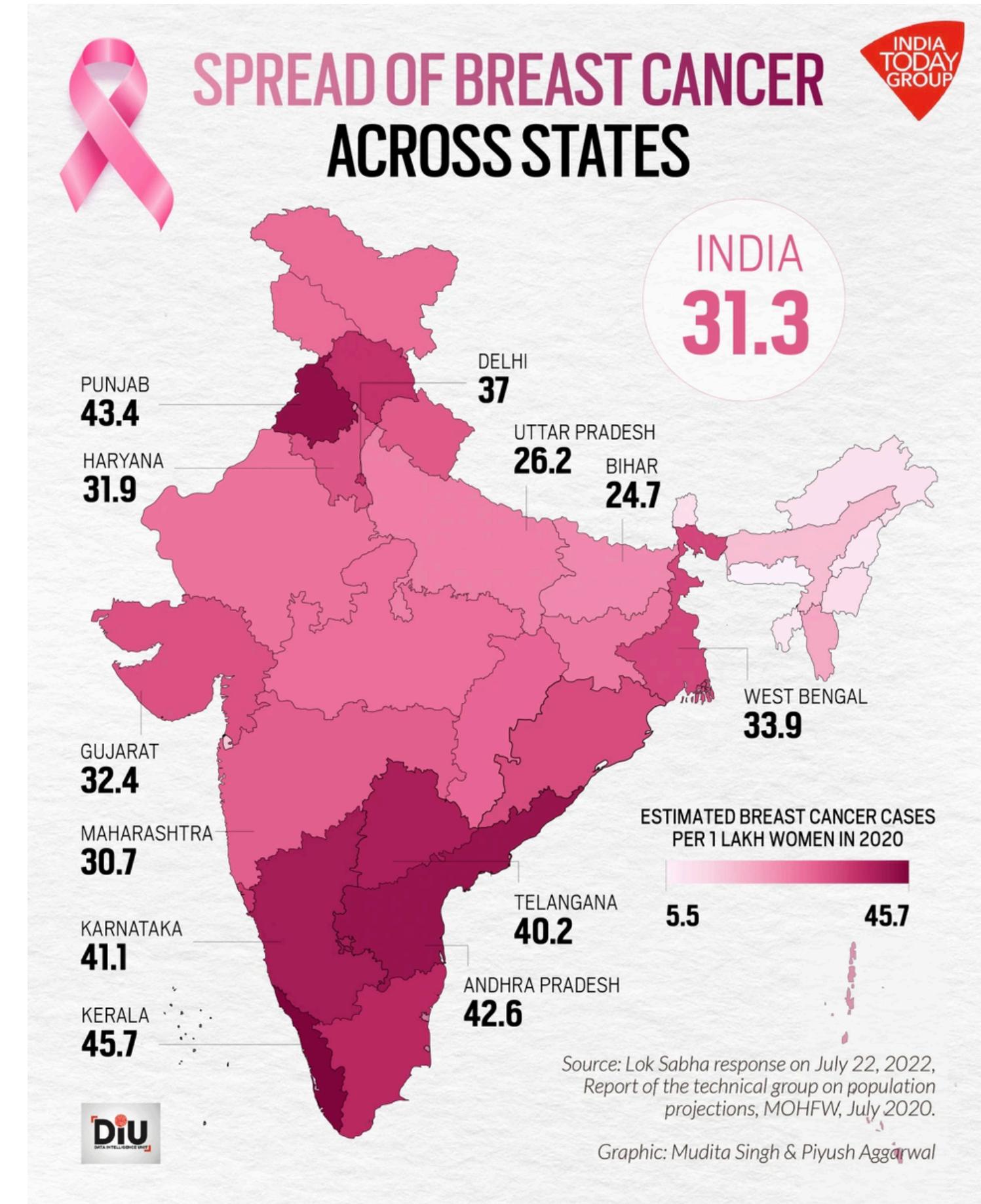
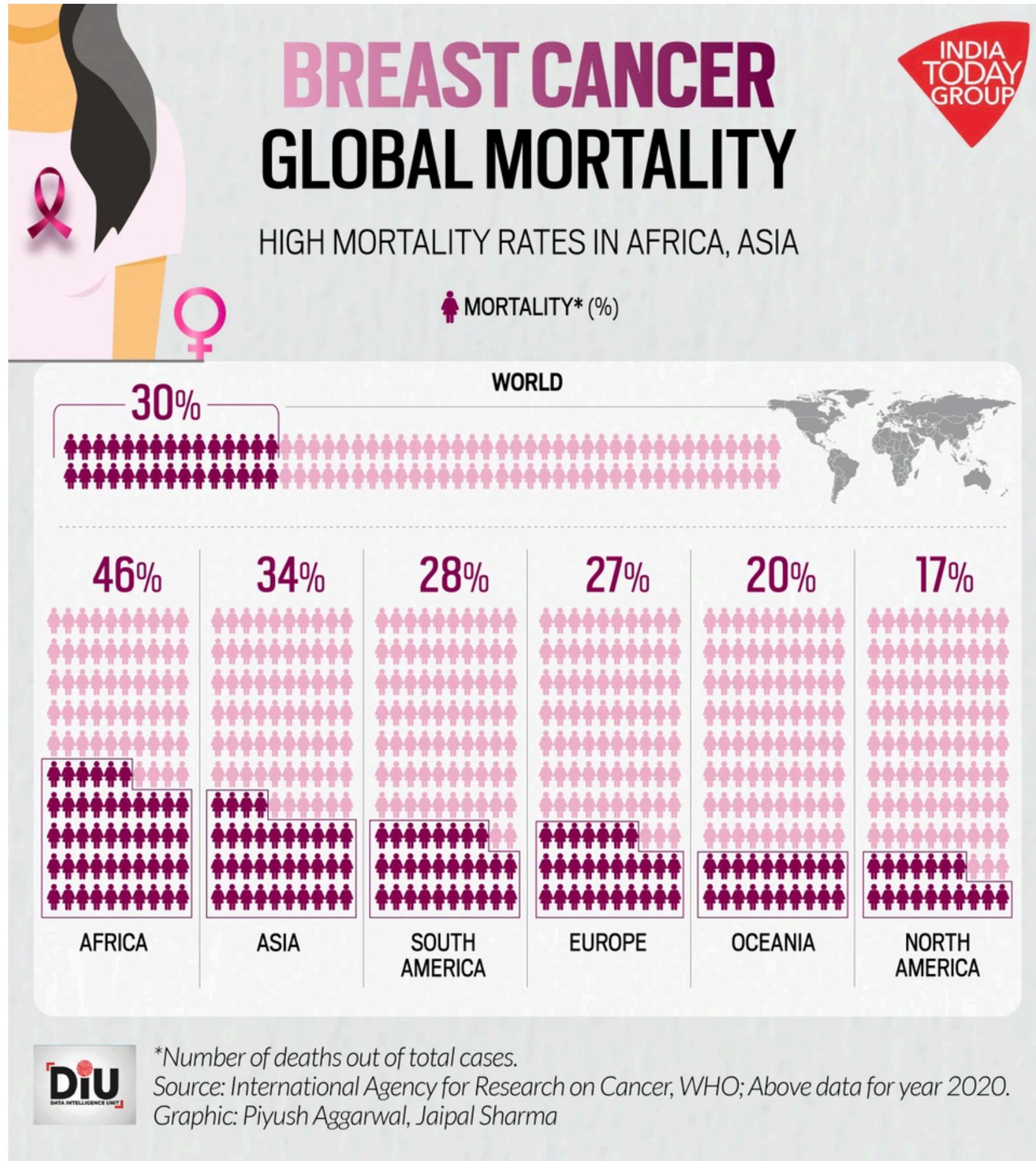
The focus of this challenge is in tumor-infiltrating lymphocytes (TILs) in Her2 positive and Triple Negative breast cancer (BC) histopathology slides. In recent years, several studies have shown the predictive and prognostic value of visually scored TILs in BC as well as in other cancer types, making TILs a powerful biomarker that can potentially be used in the clinic.



- Manual Examination
- Human Error
- Limited Professionals

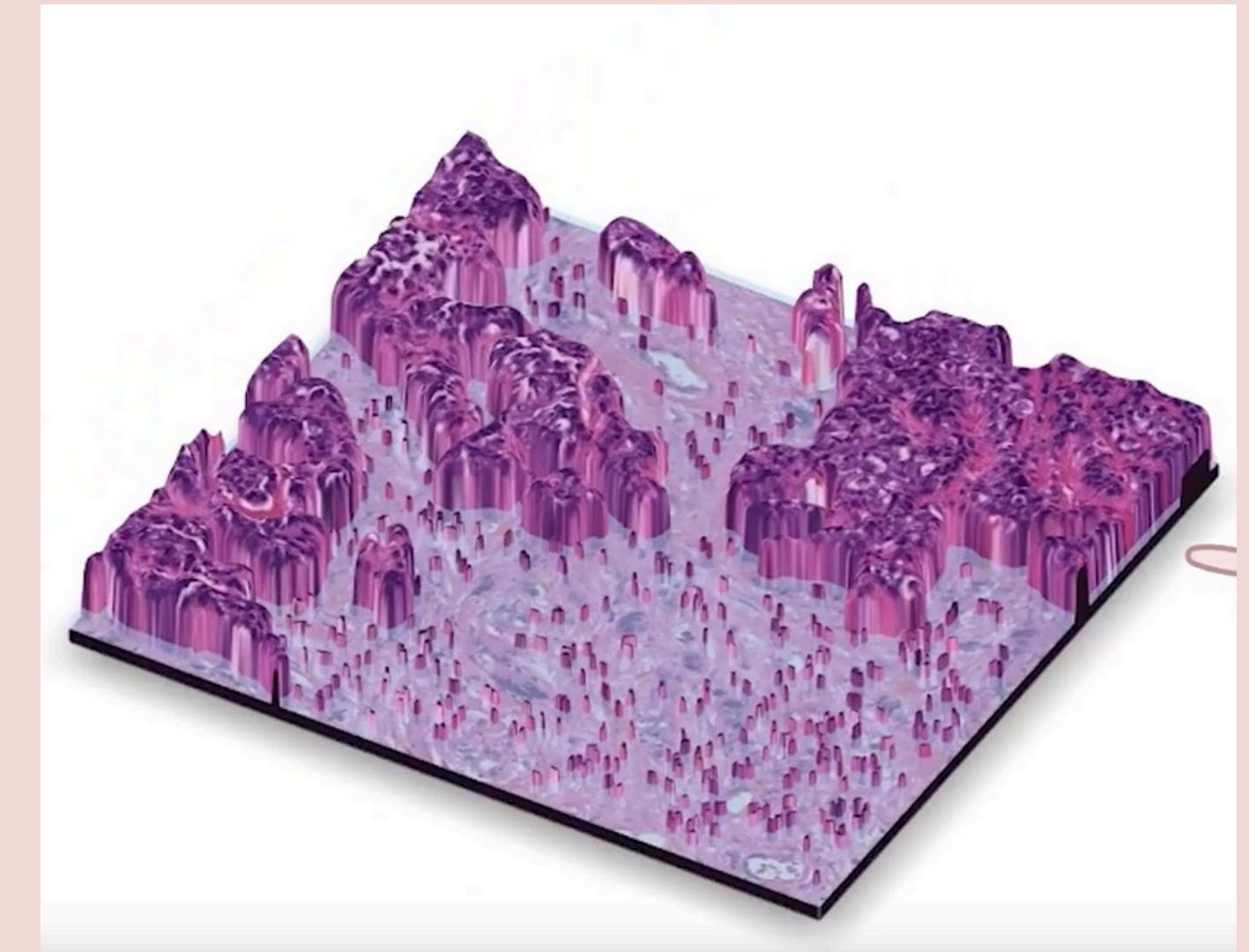
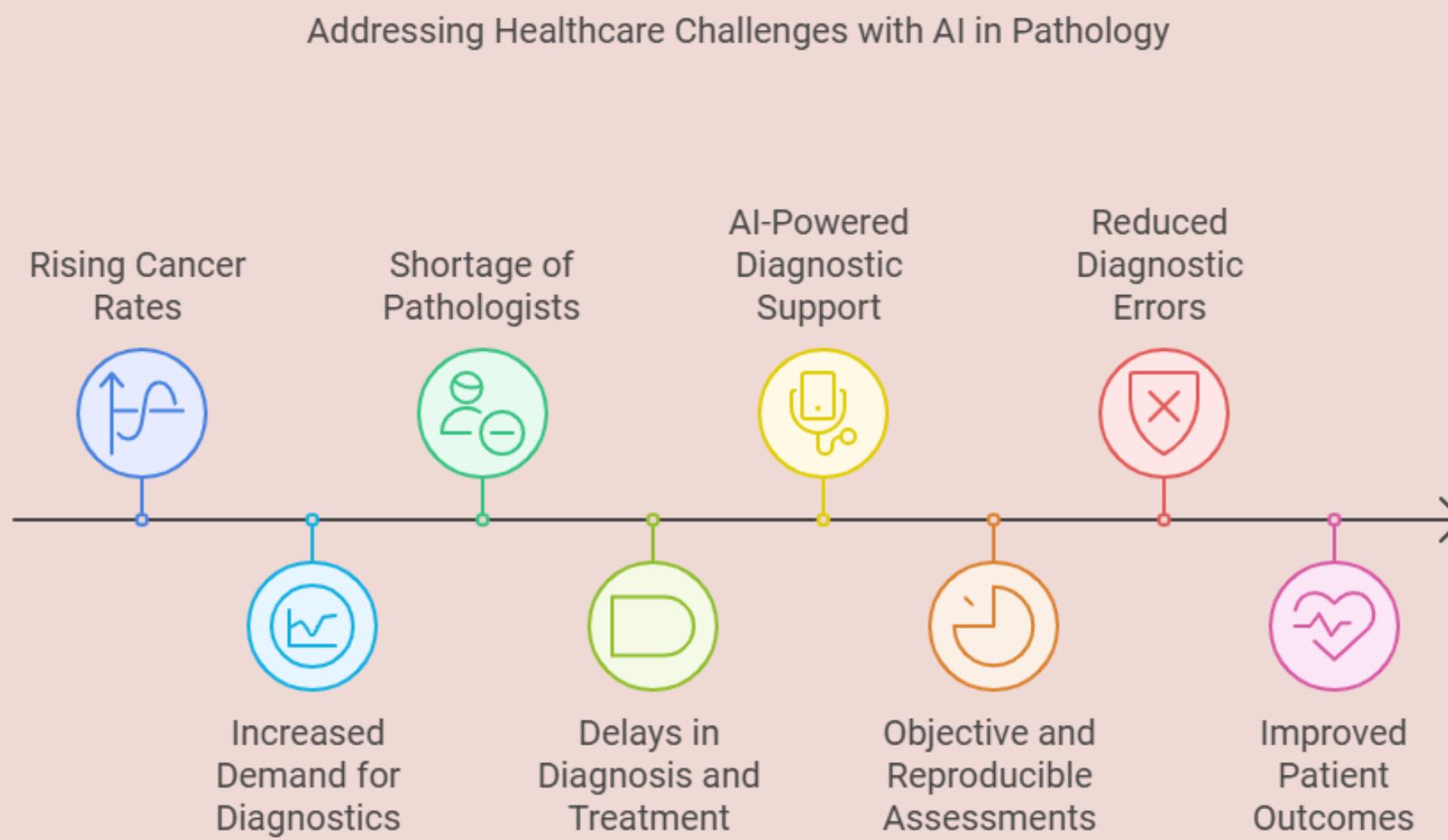


- Faster Diagnosis
- More Accurate Diagnosis
- Broader Accessibility

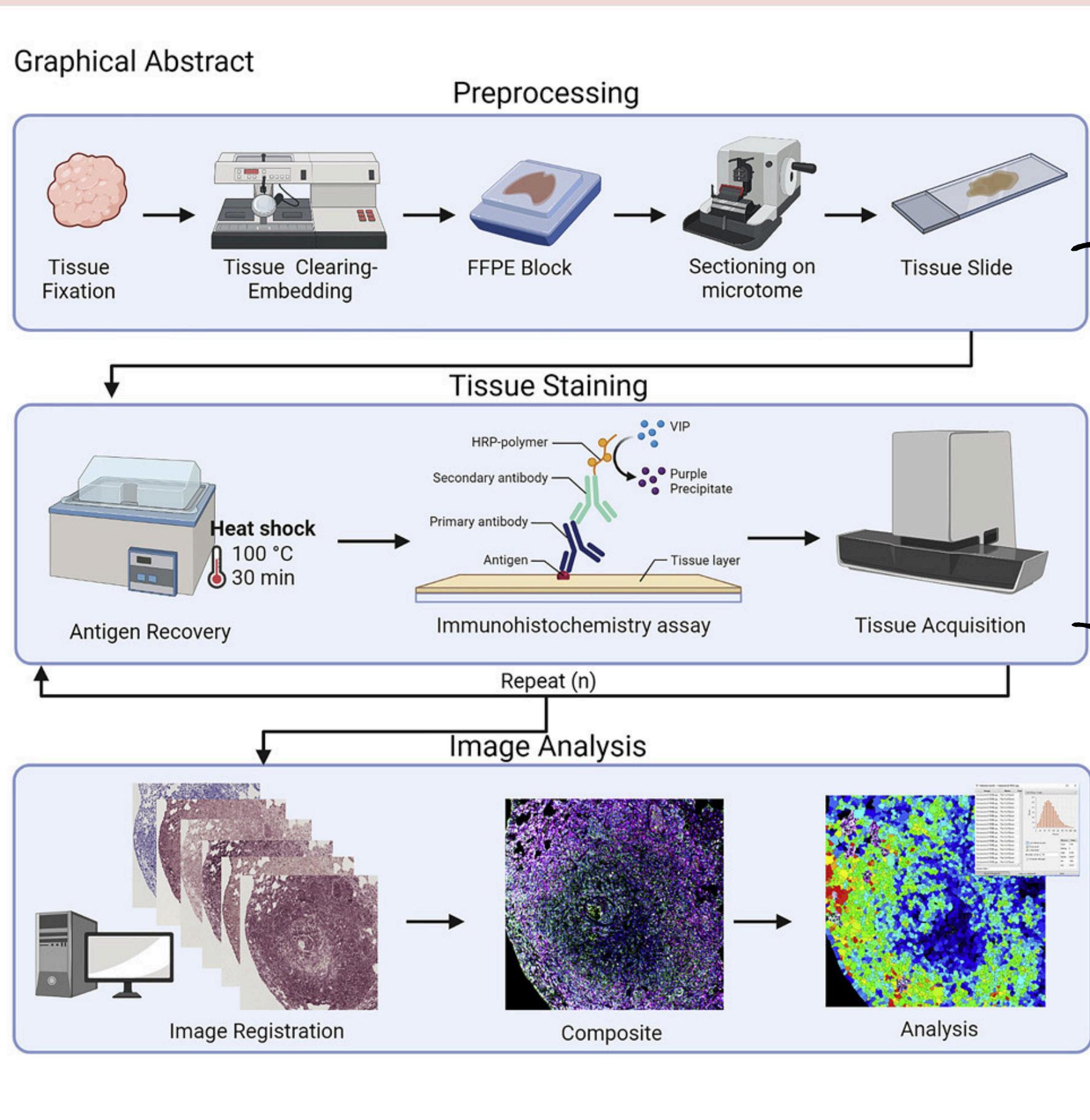


Challenges in Traditional Diagnosis

- **Manual Examination:** Pathologists manually examine histopathology slides, which is labor-intensive and subject to human error.
- **Limited Expertise:** There is a shortage of skilled pathologists, leading to delays and potential inconsistencies in diagnosis.
- **Variability:** Differences in slide quality, staining, and patient samples can affect diagnostic accuracy and consistency.



Processing Histopathology Slide

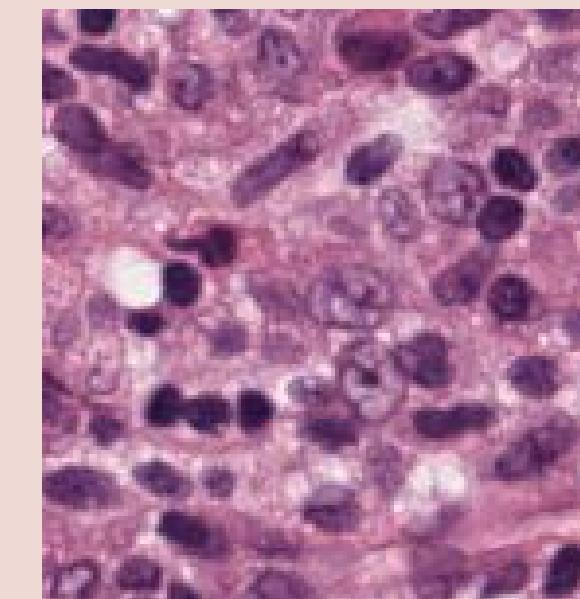
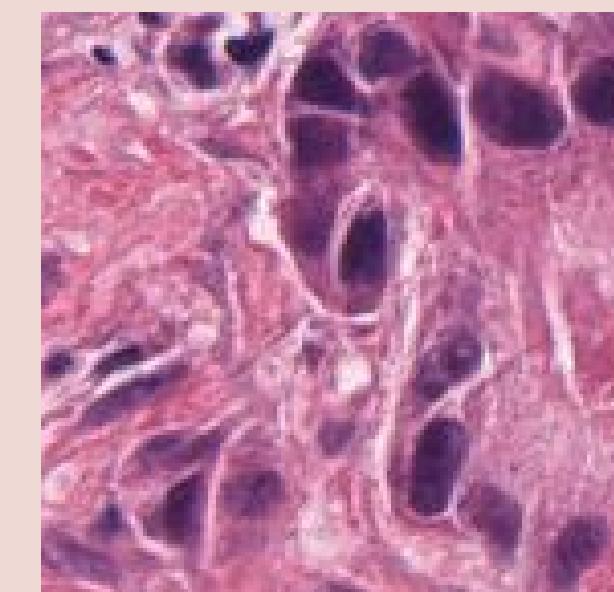
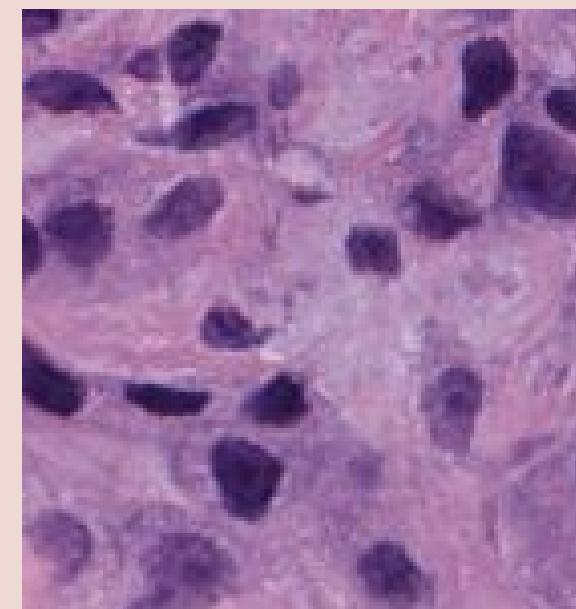
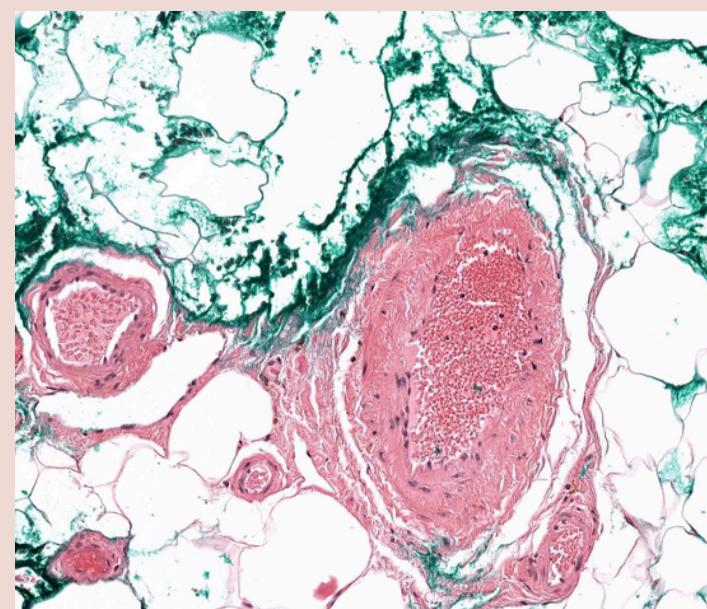
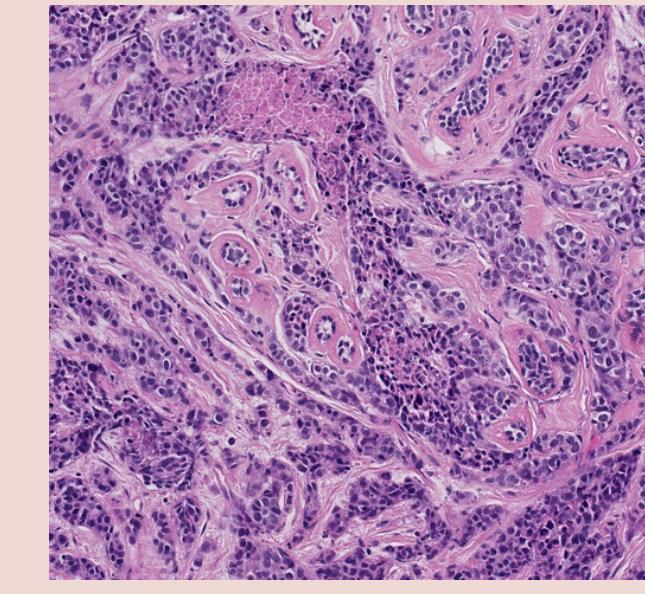
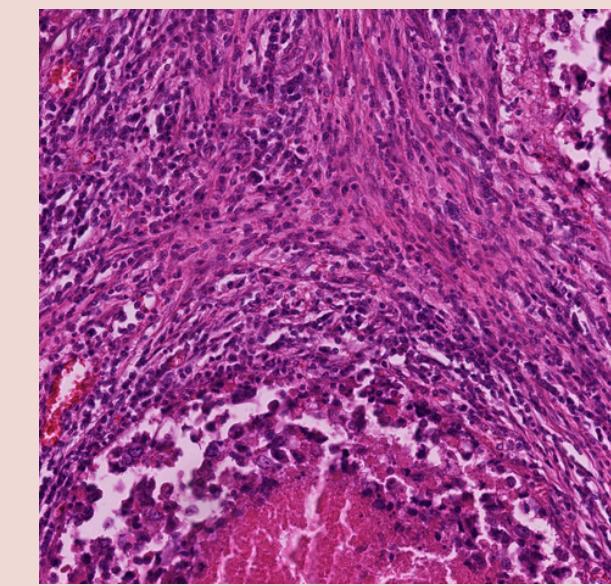
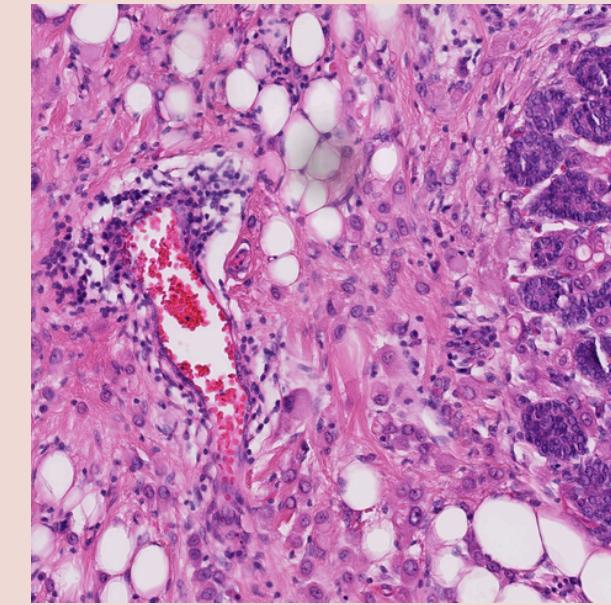
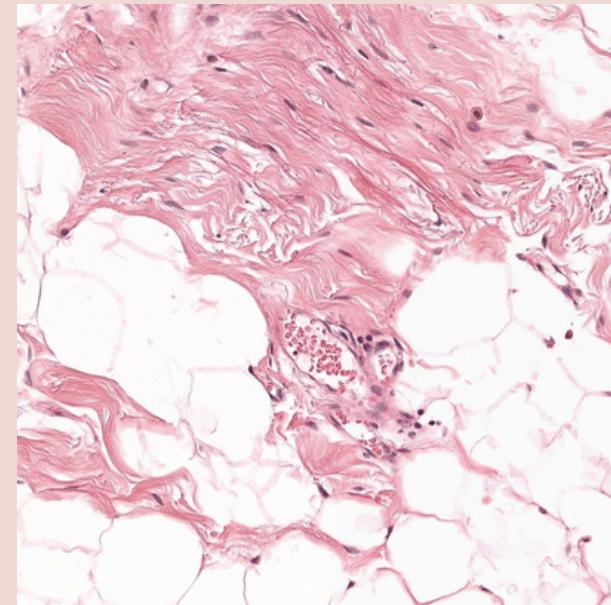
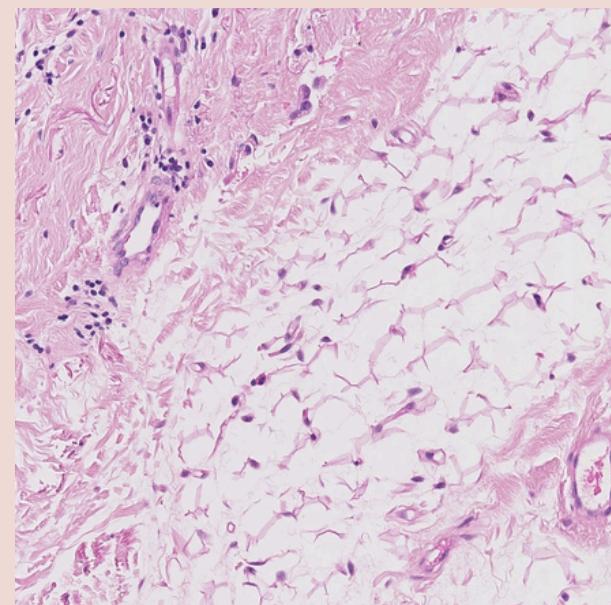


Histology slide preprocessing involves three key steps:

- (1) Tissues are fixed in **formalin**.
- (2) Fixed specimens are **trimmed and placed in labeled cassettes**.
- (3) They are **dehydrated, cleared, and embedded in paraffin wax**.

Living bacteria are nearly **colorless and lack contrast** with their aqueous surroundings, making them **hard to see**. Staining enhances the **contrast between the organisms and the background** for better visibility under a light microscope. Common staining methods include **Hematoxylin and Eosin**, along with other chemical and physical processes.

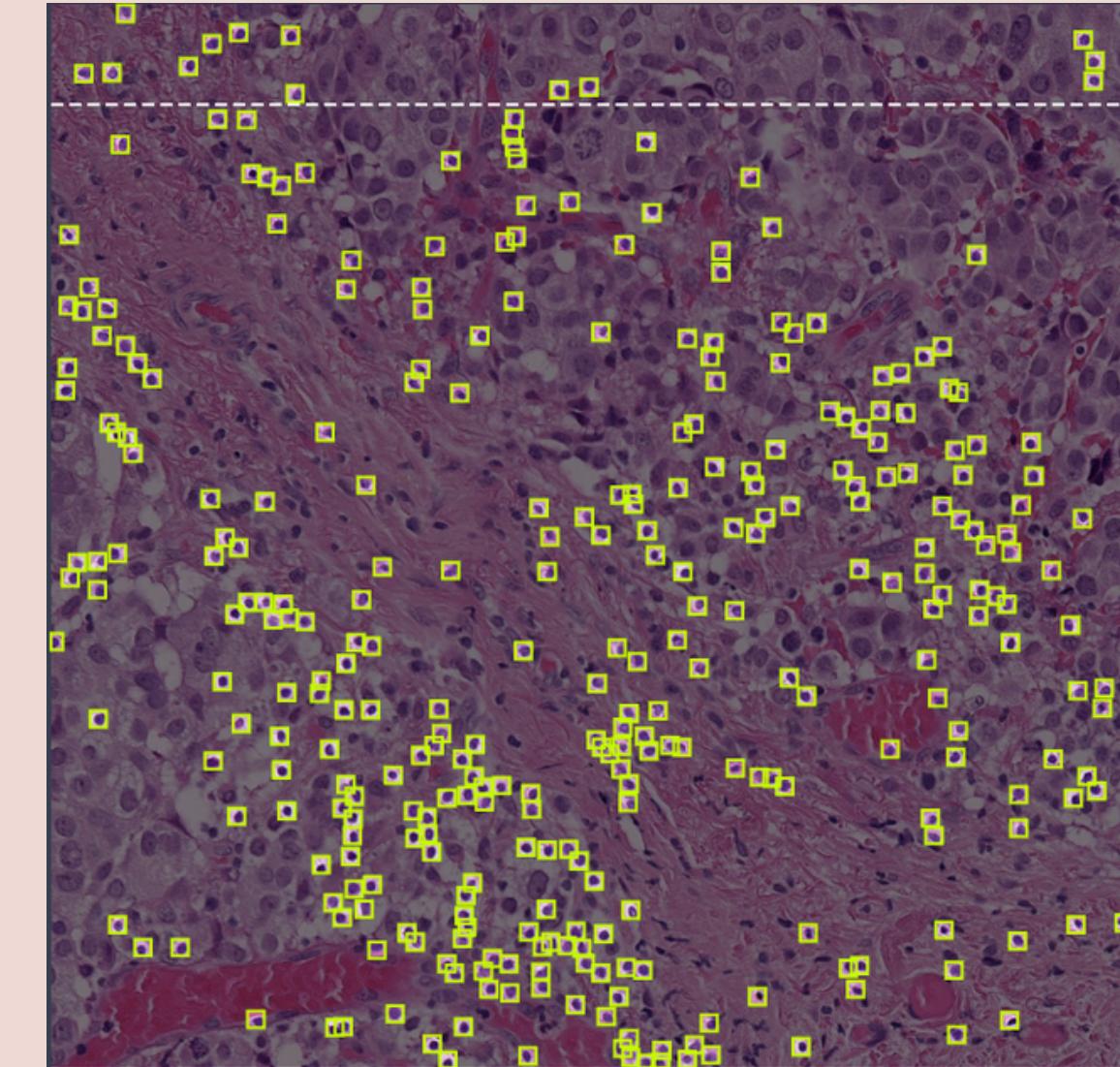
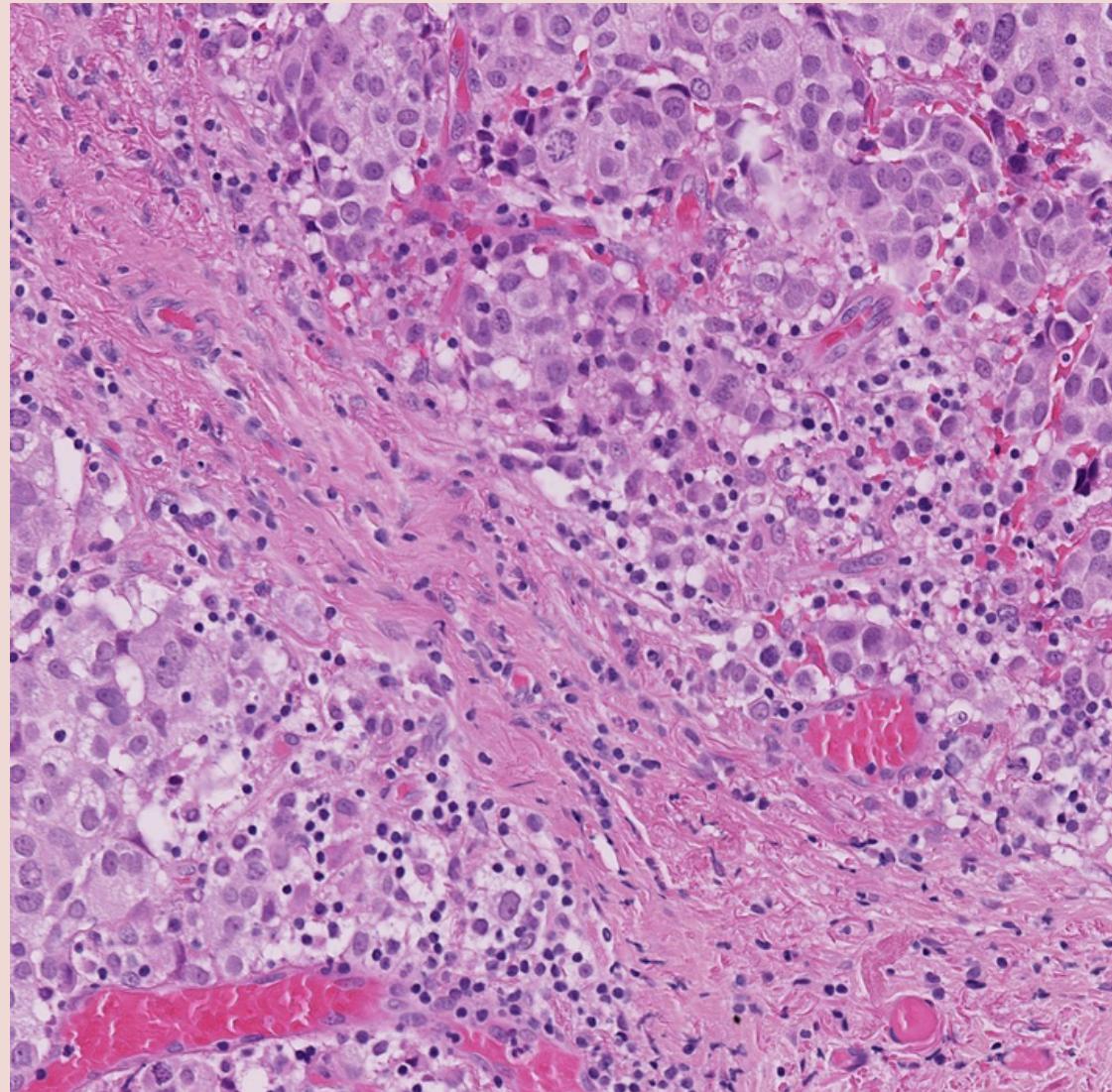
Addition of Stain in patches



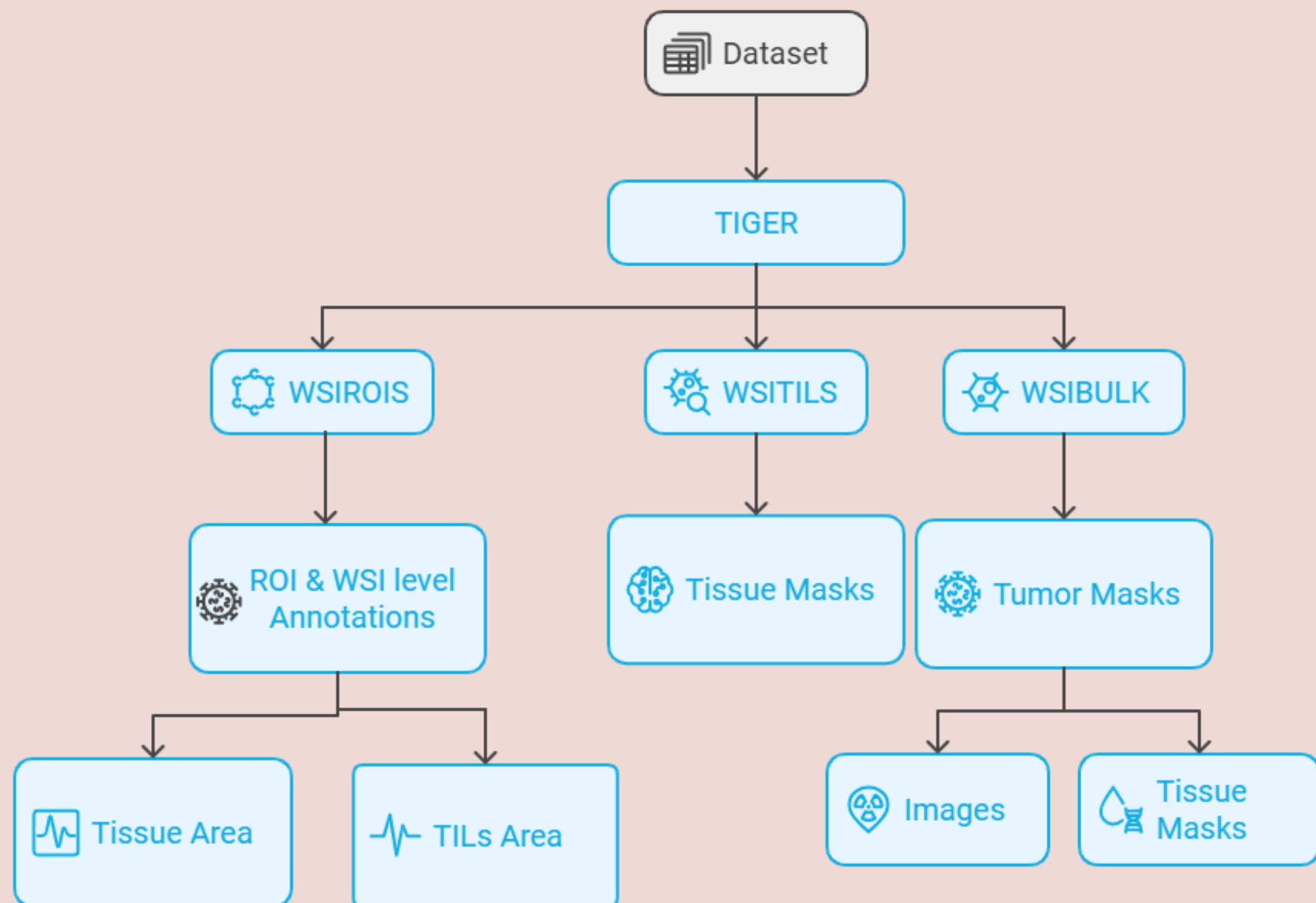
What are TILs?

Tumor-Infiltrating Lymphocytes (TILs) are immune cells that enter and accumulate in tumor tissues.

- **Prognostic Value:** Higher TIL levels are associated with better survival rates and a stronger immune response against the tumor.
- **Predictive Value:** Elevated TILs predict improved outcomes with immunotherapy and may reduce the need for aggressive treatments like chemotherapy.



DATASET



wsibulk: Contains whole-slide images (WSIs) and manual annotations for tumour bulk and tissue-background masks, provided in formats: TIF, XML.

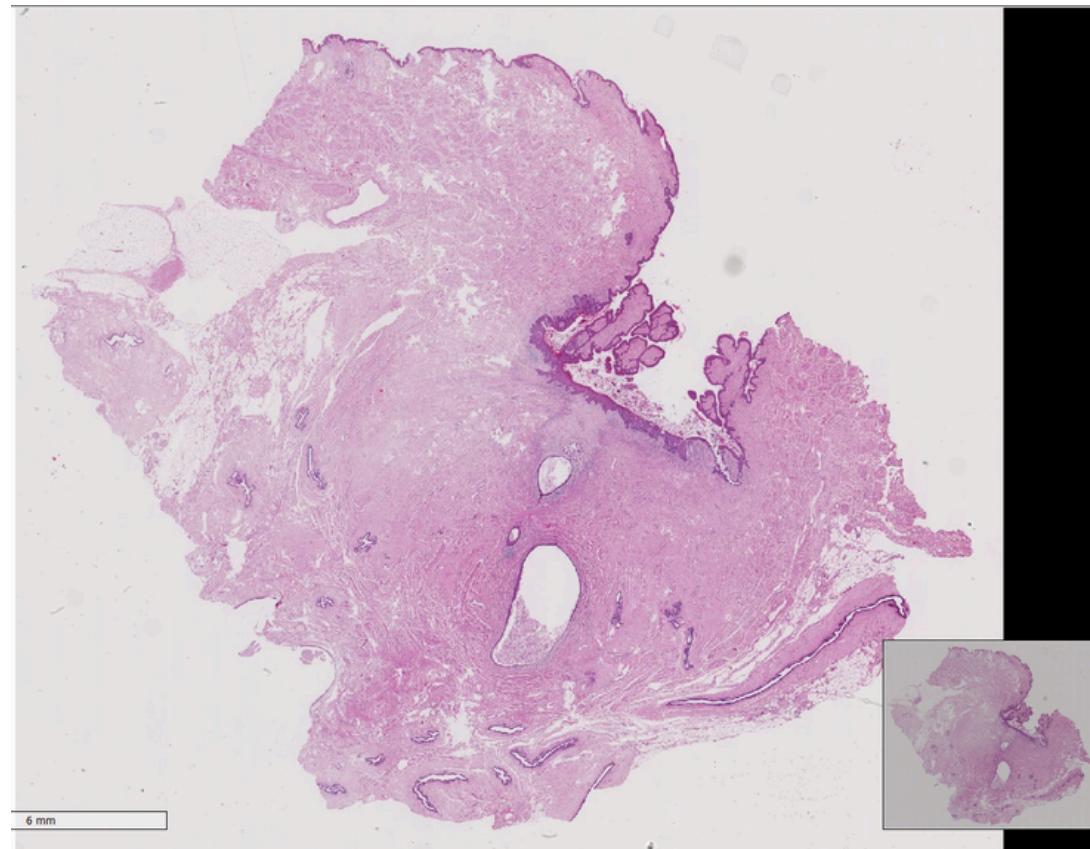
wsirois: Includes cropped regions of interest (ROIs) with detailed annotations for tissue and cells, including images and masks in PNG format, and cell annotations in COCO format.

wsitils: Comprises whole-slide images, tissue-background masks, and TIL scores in CSV format for evaluating automated TIL scoring models.

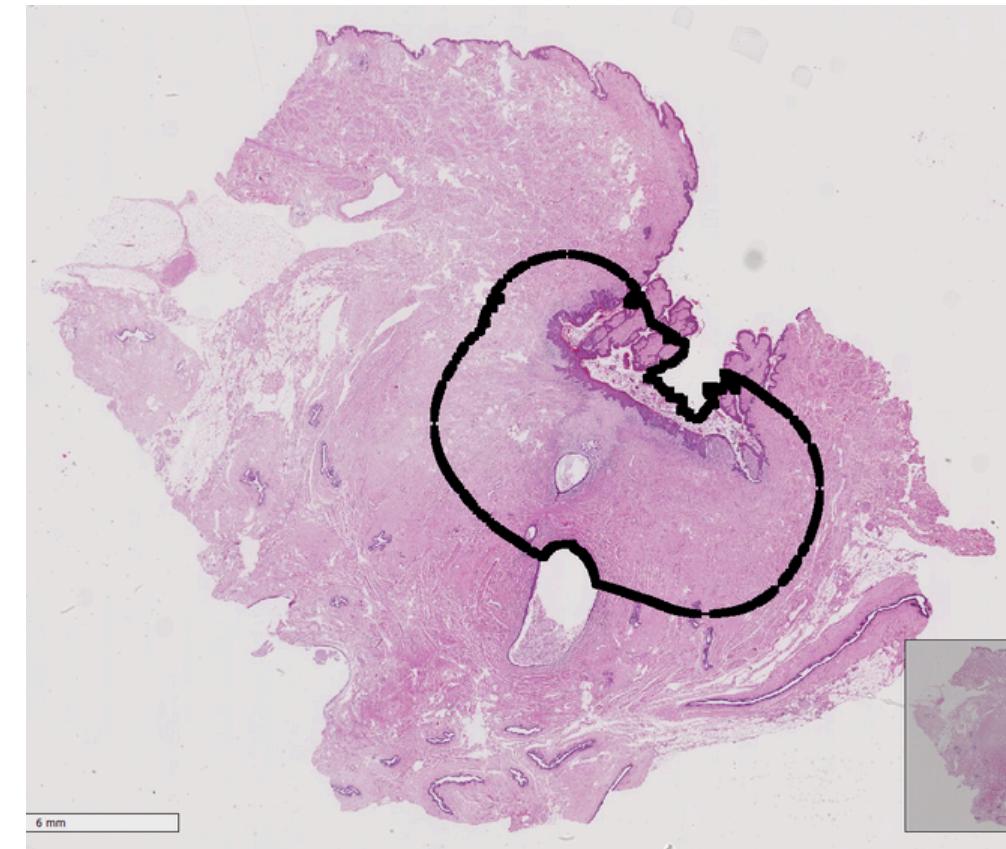
WHOLE SLIDE IMAGE

Whole-slide images (WSIs) are high-resolution digital scans of entire histopathology slides, capturing the entire tissue section from a microscope slide.

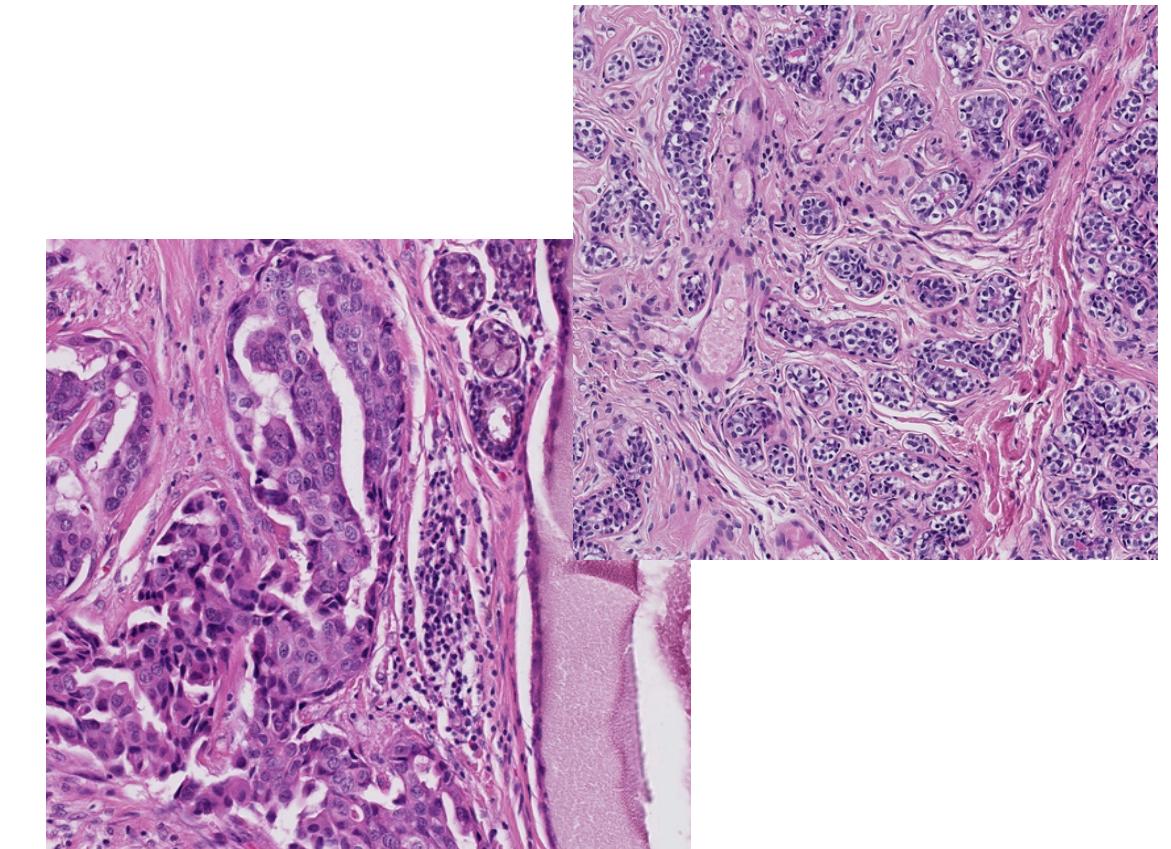
- **High Resolution:** Provides detailed visualization at various magnification levels.
- **Large File Size:** Contains a massive amount of data due to high resolution and large tissue area.



WSI

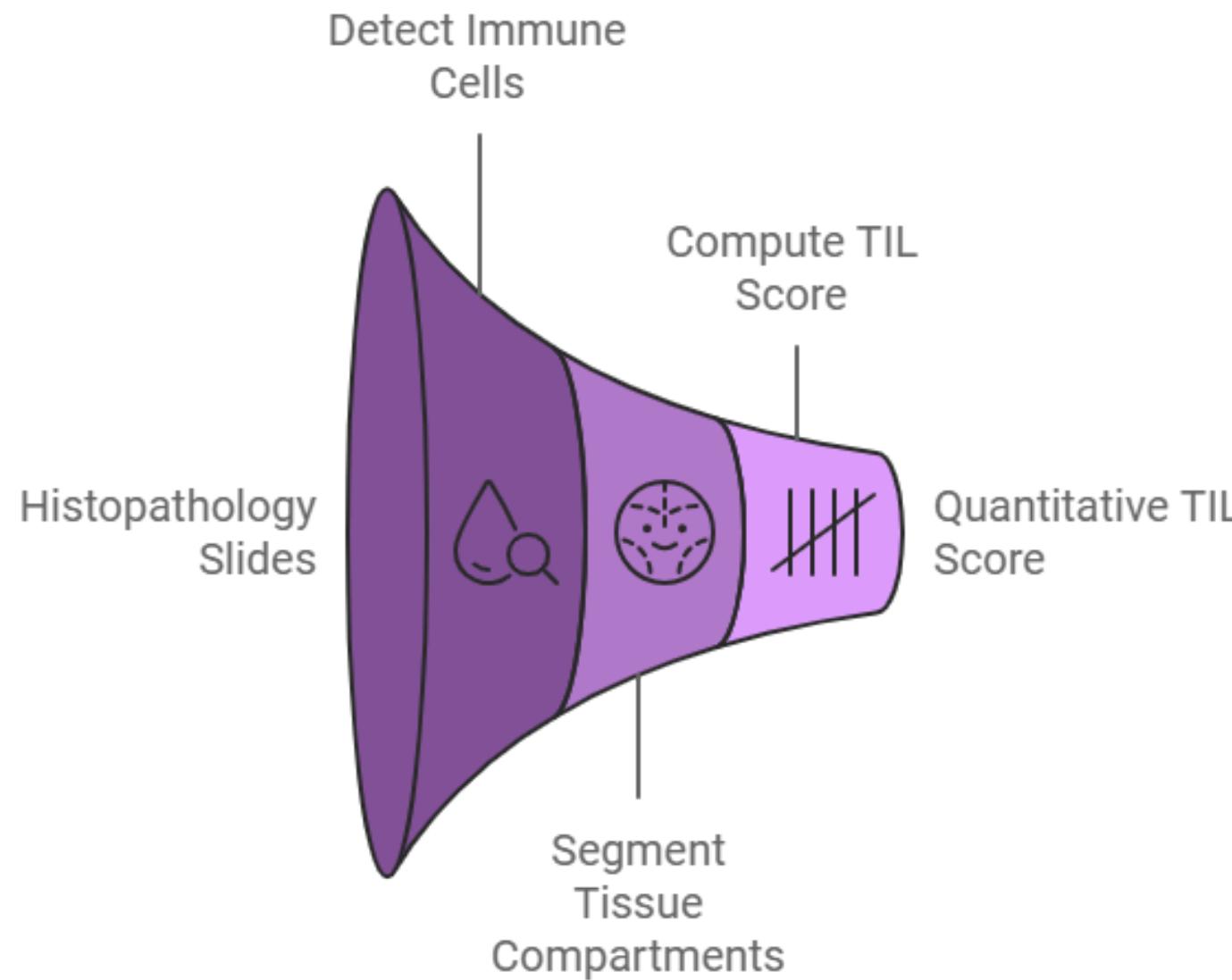


WSI Mask



PATCHES

TASKS IN THE TIGER CHALLENGE



1. Detection of Lymphocytes and Plasma Cells

Objective: Identify and classify the key immune cells involved in TILs.
Focus: Lymphocytes (T cells and B cells) and plasma cells.

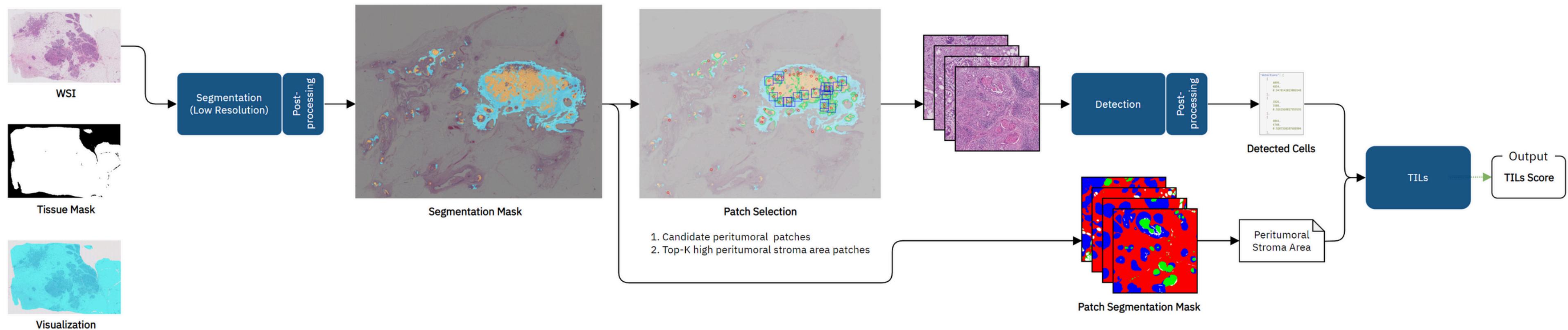
2. Segmentation of Invasive Tumor and Tumor-Associated Stroma

Objective: Accurately segment the tissue compartments in the histopathology slides.
Focus: Distinguish between invasive tumor and tumor-associated stroma.

3. Computation of Automated TIL Score

Objective: Generate a quantitative TIL score for each slide.
Focus: Integrate detection and segmentation results to compute the TIL score.

PIPELINE



APPROACH

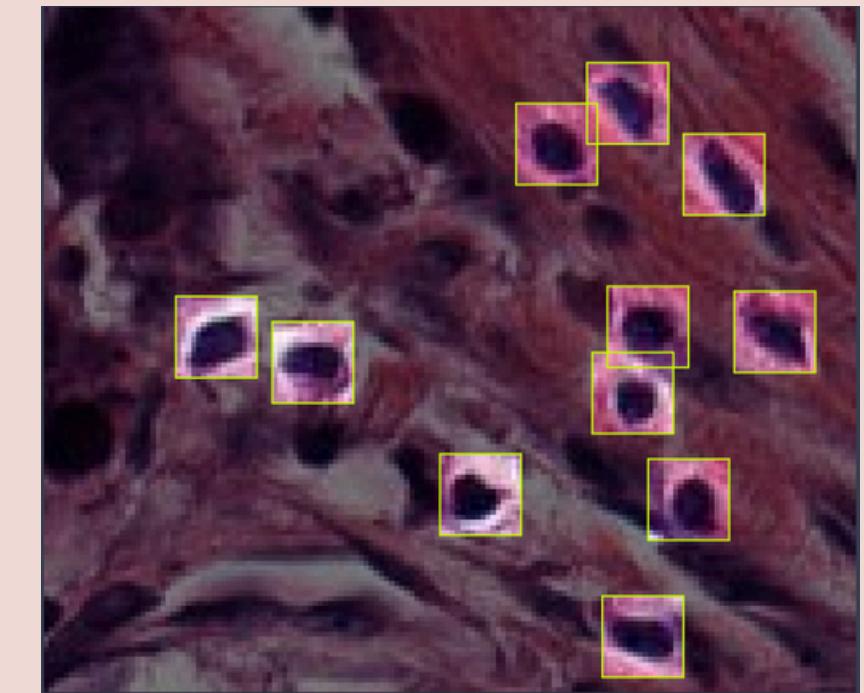
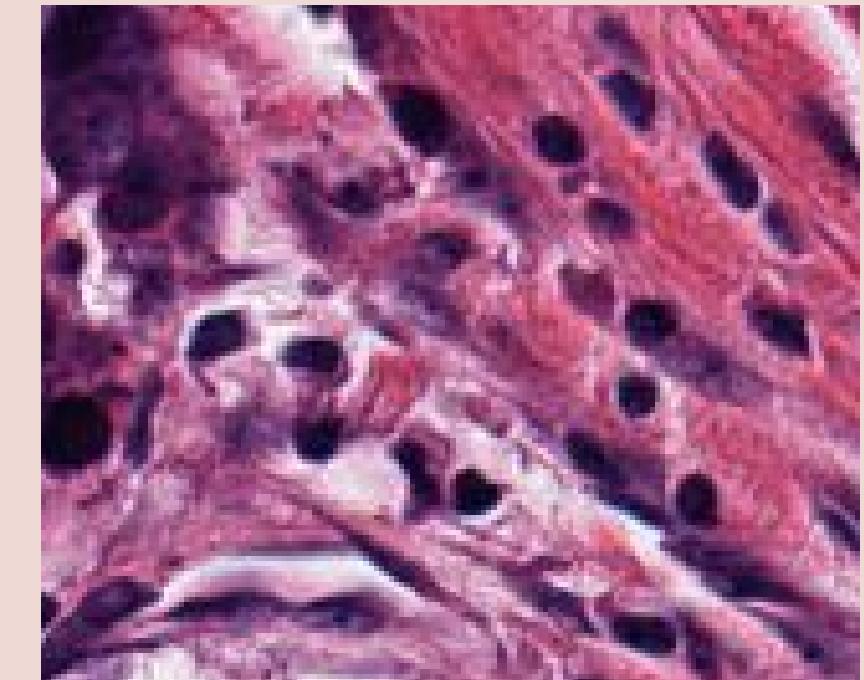
Detection of Lymphocytes and Plasma Cells

Preprocessing Steps

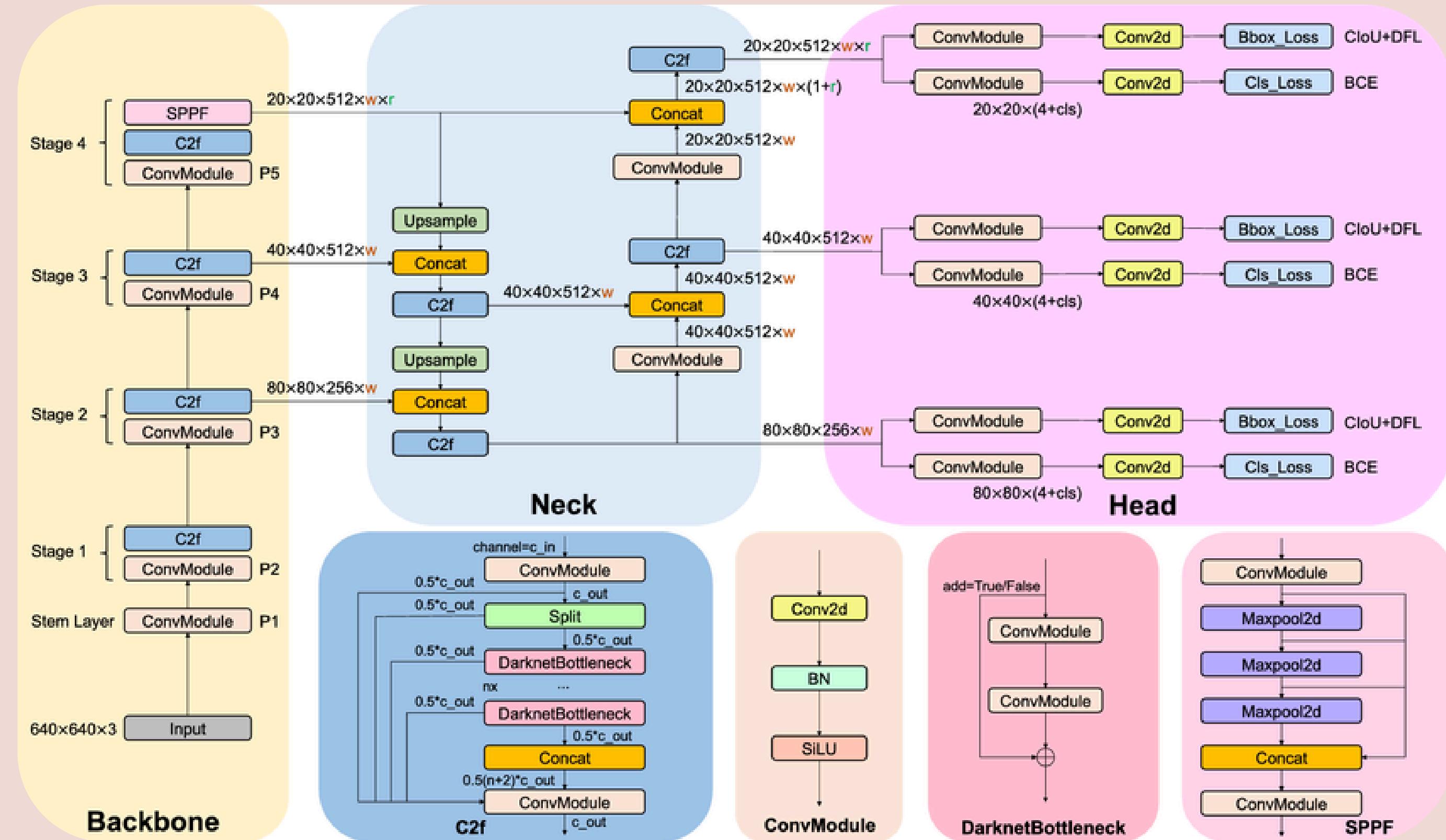
- **Image Resizing:**
 - **Size:** Resized all images to **512x512 pixels** for consistent input size.
- **Annotation Application:**
 - **Source:** Used COCO format annotations from coco.json for lymphocytes and plasma cells.
 - **Conversion:** Conversion of annotations from json to yolov8 supportable format.
 - **Application:** Applied annotations to 1,879 images to create a labeled dataset.

Model Training

- **Algorithm: YOLOv8 Detection Model**
 - **Training:** Utilized preprocessed images with applied annotations.
 - **Parameters:** Adjusted various parameters to optimize model performance.

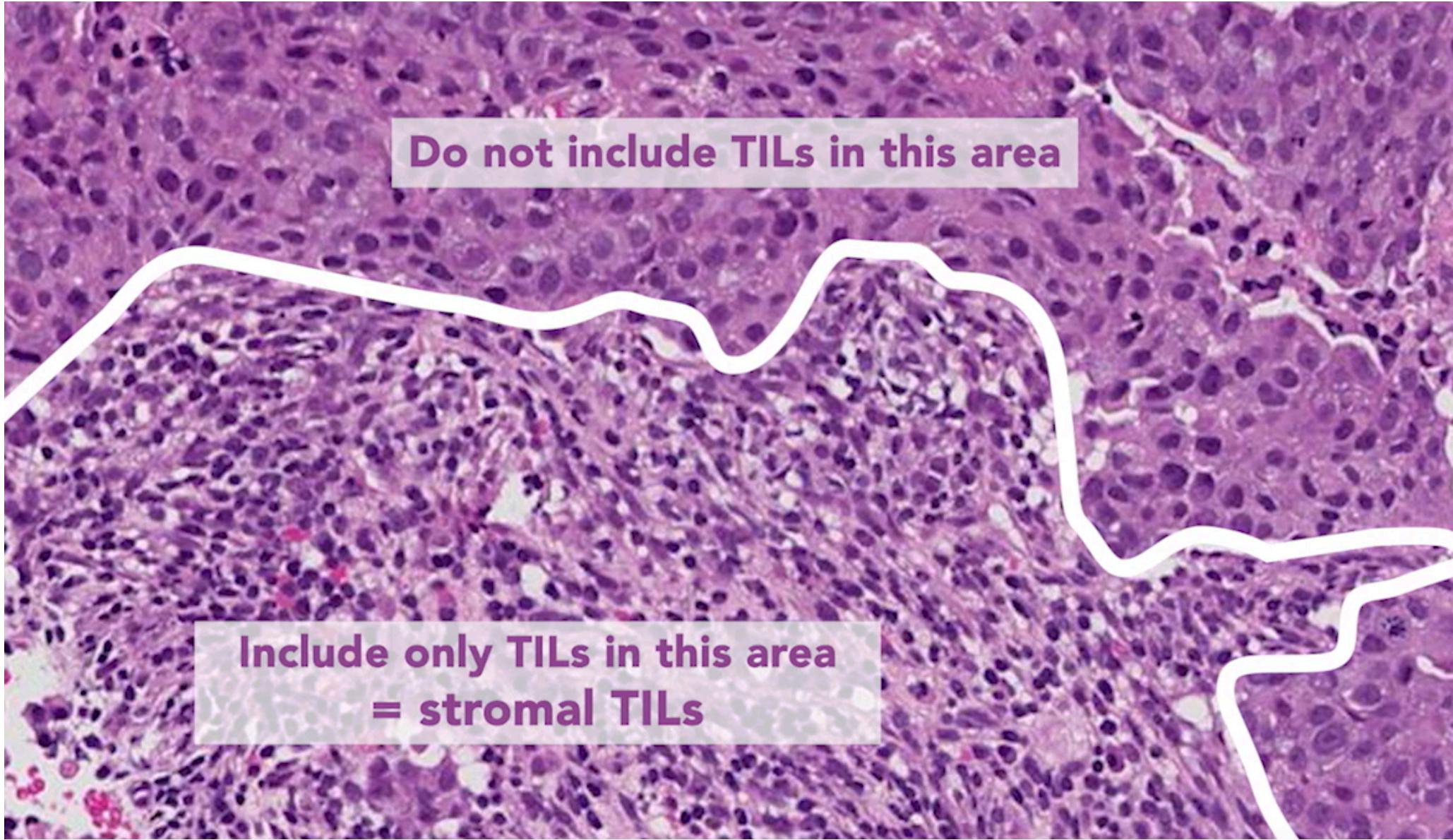


YOLOv8 Detection Model



YOLOv8 is a state-of-the-art object detection model known for its real-time performance and high accuracy. It uses a deep neural network with a balance of speed and precision, making it ideal for detecting lymphocytes and plasma cells in medical images.

Segmentation of Invasive Tumor and Tumor-Associated Stroma



- **Image Preprocessing:** Images are split into 512x512 patches to retain crucial details and avoid feature loss during segmentation.
- **Color/Stain Normalization:** Adjusts color variations in histopathology images to improve consistency, using Hematoxylin and Eosin stain normalization.
- **Model & Training:** Efficient-UNet model with separate learning rates for encoder/decoder, trained over 70 epochs using Jaccard Loss to segment tumor and stroma regions.

Invasive Tumor (Label=1): Represents invasive tumor regions, such as invasive ductal carcinoma and invasive lobular carcinoma.

Tumor-Associated Stroma (Label=2): Includes connective tissue surrounding or within the tumor bulk.

In-Situ Tumor (Label=3): Refers to non-invasive malignant lesions, like ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS).

Healthy Glands (Label=4): Regions of glands containing healthy epithelial cells.

Necrosis Not In-Situ (Label=5): Necrotic tissue not considered part of in-situ tumors.

Inflamed Stroma (Label=6): Tumor-associated stroma with a high density of lymphocytes, crucial for assessing TILs.

Rest (Label=7): Includes any remaining tissue compartments not annotated, such as healthy stroma, erythrocytes, adipose tissue, and skin.

We changed the mask values as follows: [0→0, 1→1, 2→2, 3→0, 4→0, 5→0, 6→2, 7→0], 0 corresponds to the rest class, 1 the tumor class and 2 the stroma class:

	ROI
0	Invasive Tumor
1	Tumor Associated Stroma
2	In-situ Tumor
3	Healthy Glands
5	Necrosis not in-situ
6	Inflamed Stroma
7	Rest

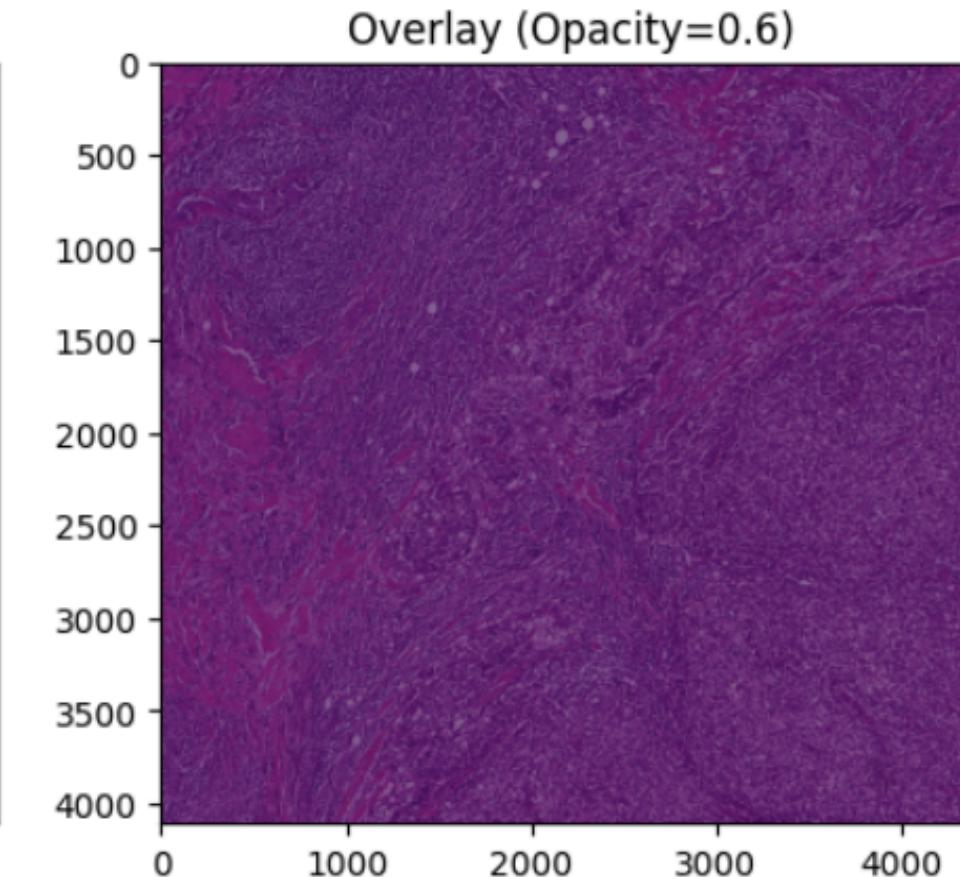
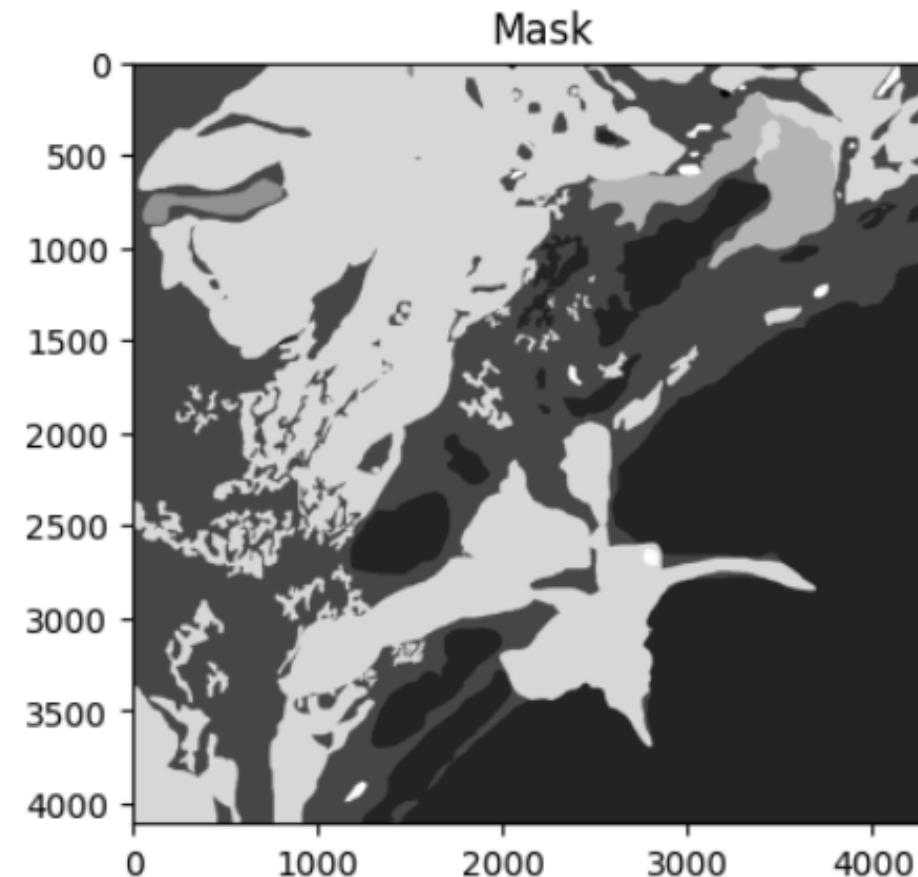
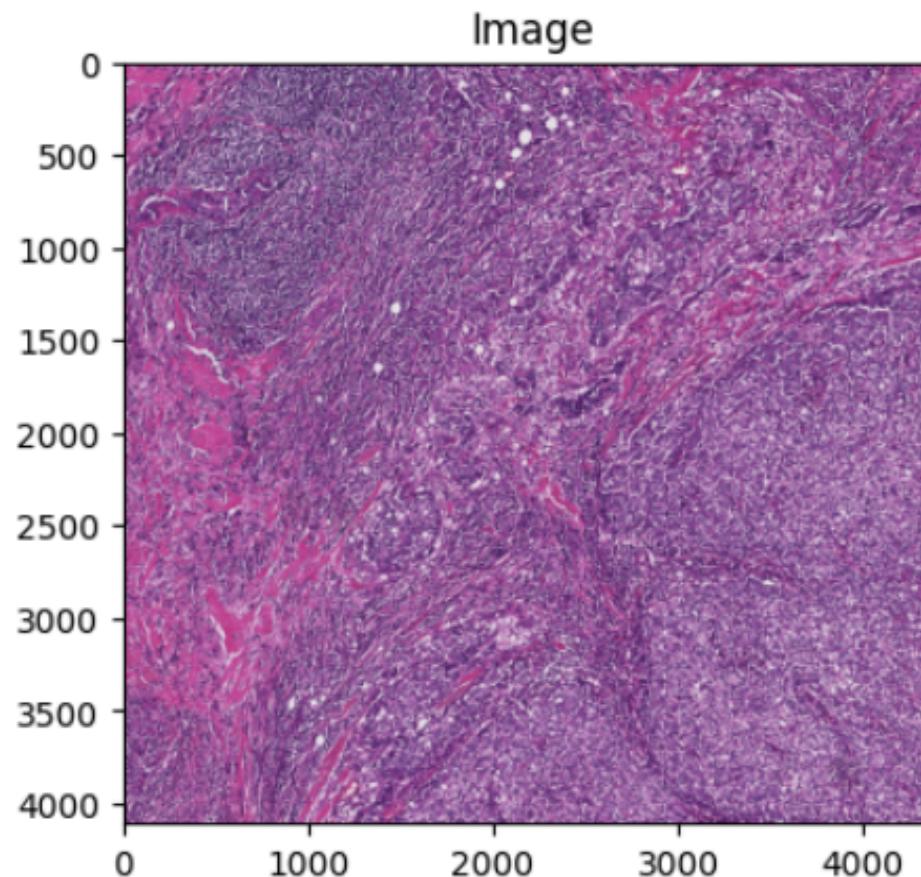
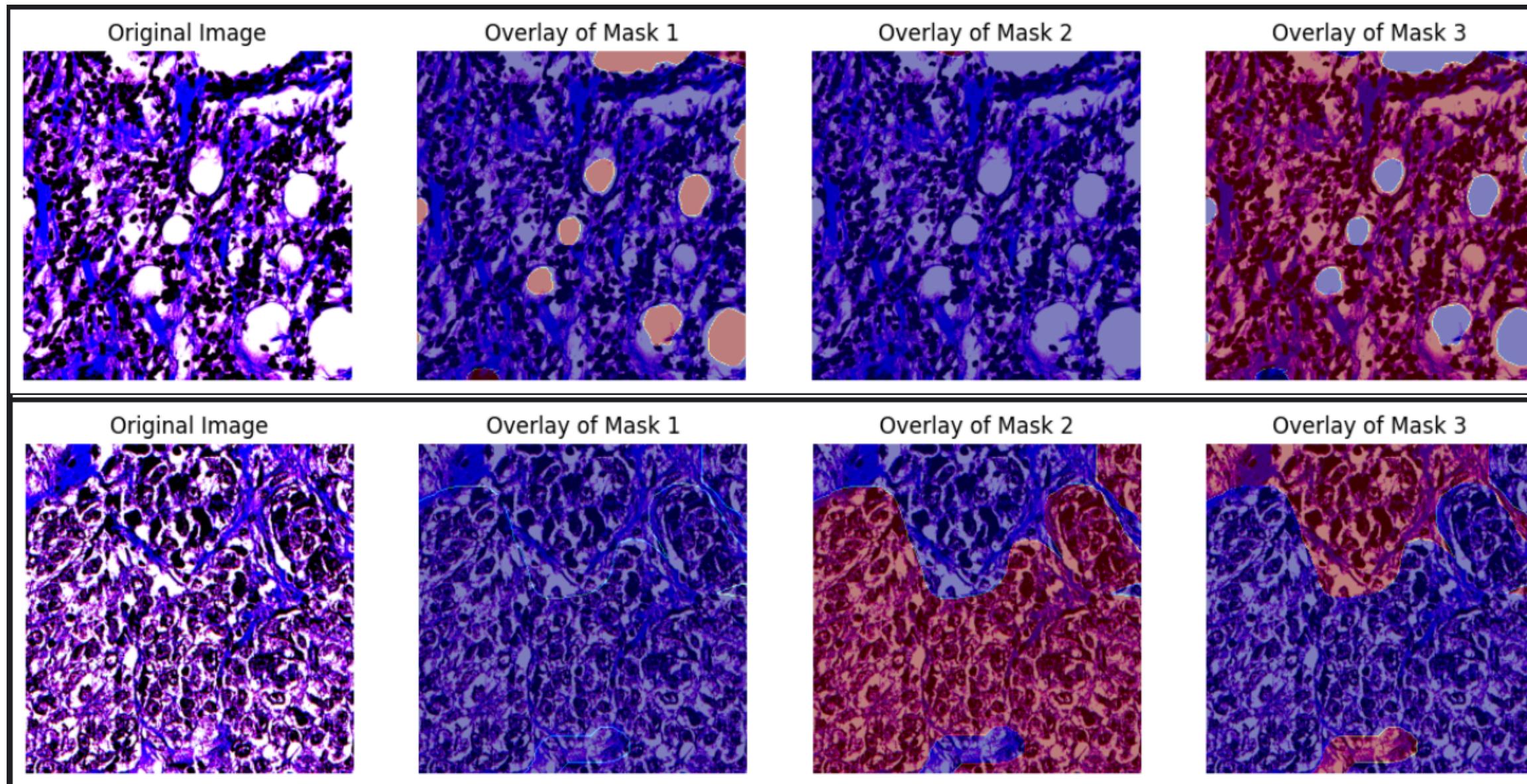


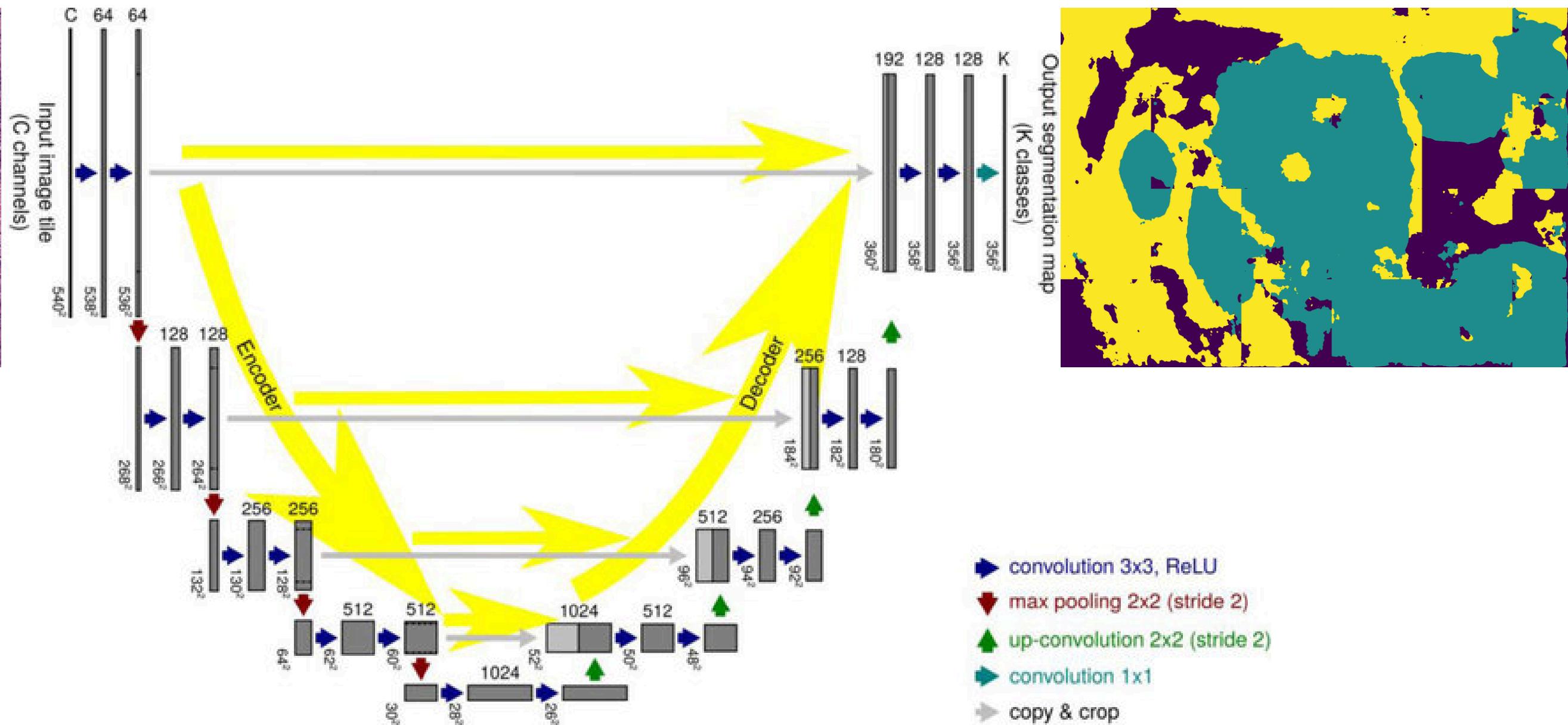
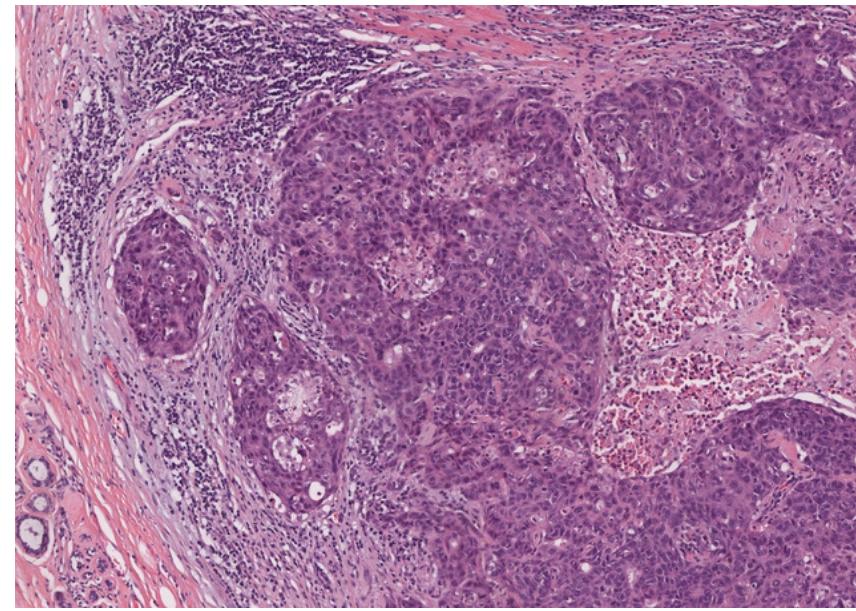
Image and Masks Preprocessing Steps

1. Patch Generation: Create 256×256 patches from the larger images.
2. Normalization: Normalize all patches to ImageNet weights, as we are using a pretrained UNET backbone.
3. Mask Preparation: Remove unnecessary channels and labels from the masks, as demonstrated in previous slides.
4. Stain Normalization: Apply stain normalization to all images.
5. Center Cropping: Perform center cropping on each patch and add extra padding if the patch falls short in size.



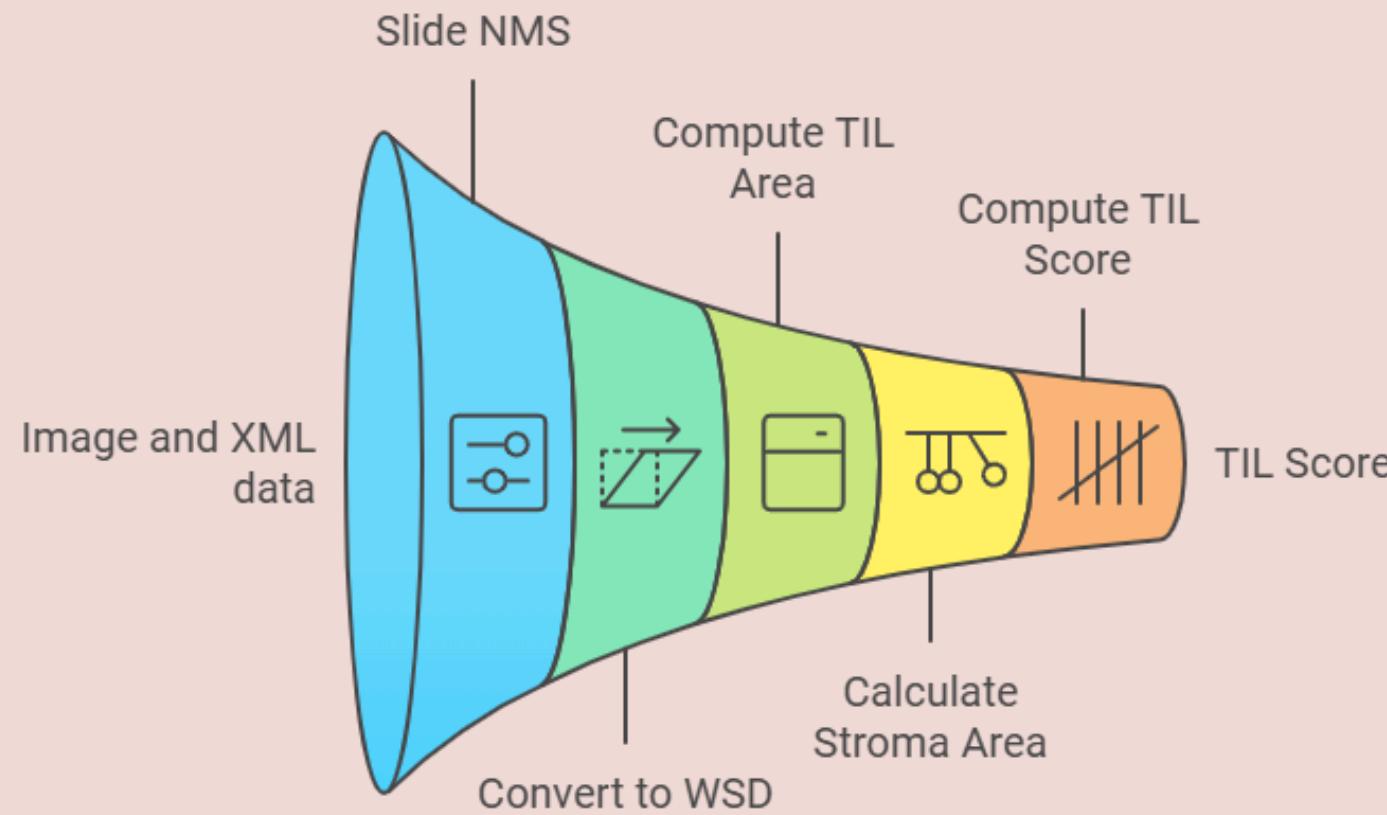
Summary of Model Training

- **Backbone Selection:** Various backbones, including **EfficientNetBo**, **EfficientNetB7** and **InceptionV3** were used for segmentation models. The choice of backbone affects feature extraction and is based on performance with pre-trained weights, especially when image data is limited.
- **Training Strategy:** A **two-phase training** approach was adopted to manage the learning process and reduce overfitting, crucial for small datasets.
 - a. **Phase 1 (Freeze the Encoder):** The encoder is frozen to train only the decoder and head, preventing premature updates to the backbone's pre-trained weights.
 - b. **Phase 2 (Unfreeze the Encoder):** All layers are unfrozen for full network training to fine-tune the model.
- **Overfitting Mitigation:** **Dropout** was used to **randomly deactivate** a fraction of input units during training, helping prevent **over-fitting** on specific neurons.
- **Loss Functions:** Experiments were conducted with **Dice Loss**, **Categorical Focal Loss**, and their combinations to enhance performance in imbalanced segmentation tasks by emphasizing difficult-to-classify pixels. **Class weights** were applied to Dice Loss to achieve a **balanced classification structure**.



The U-Net segmentation model is a convolutional neural network designed for precise segmentation tasks, especially in medical imaging. Its encoder-decoder architecture, with skip connections, allows it to capture both high-level context and fine details for accurate tissue segmentation.

Computation of Automated TIL Score



Determine TIL Area: The area of a single TIL in pixels based on its size in micrometers and pixel size.

Total TIL Area: Multiply the number of detected TILs by the area of a single TIL.
Stroma Area Measurement:

Measure Stroma Area: Calculate the area of tumor-associated stroma using the provided mask.

$$\text{TIL Score} = \left(\frac{100 \times \text{Total TIL Area}}{\text{Stroma Area}} \right)$$

Where:

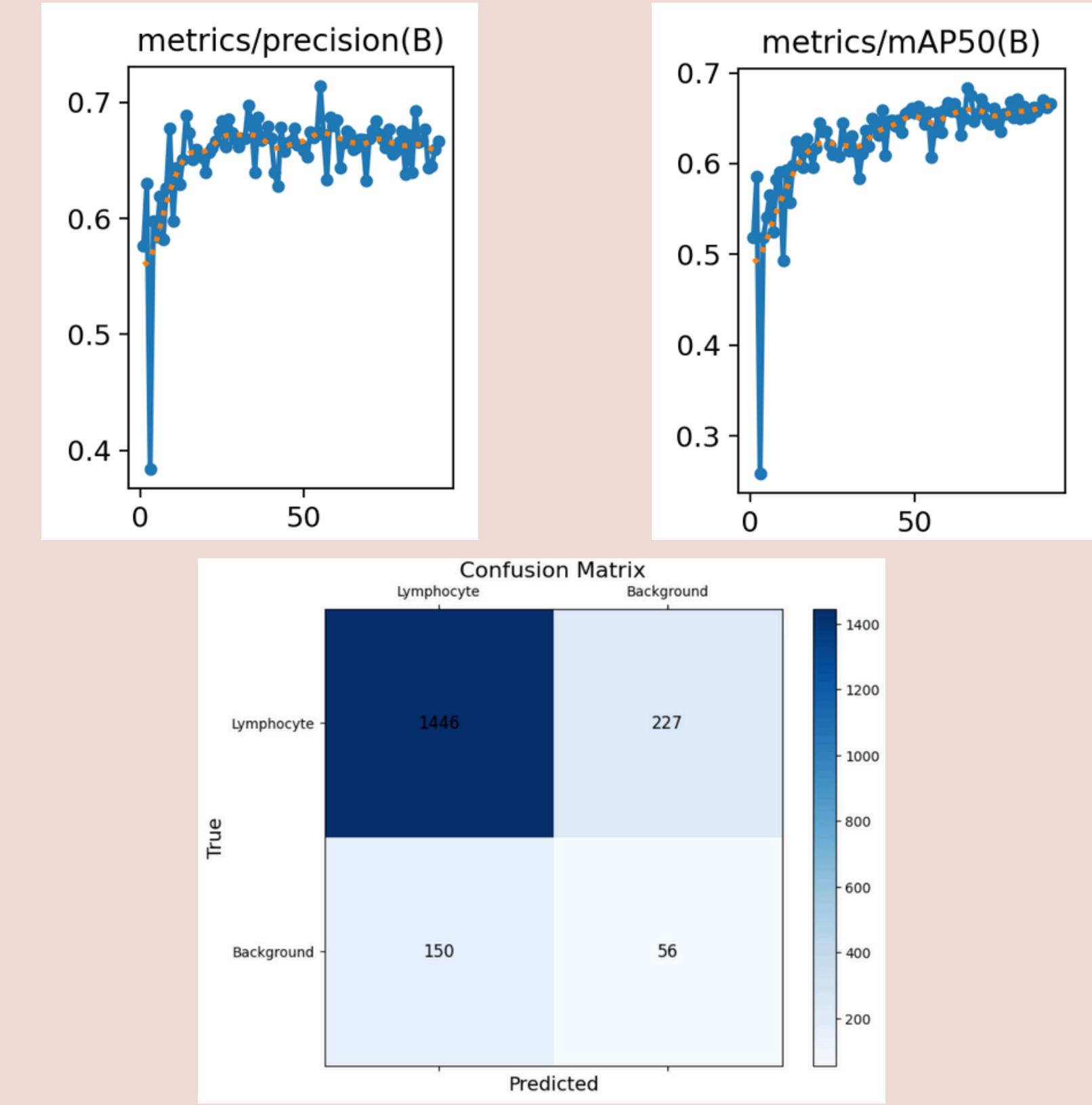
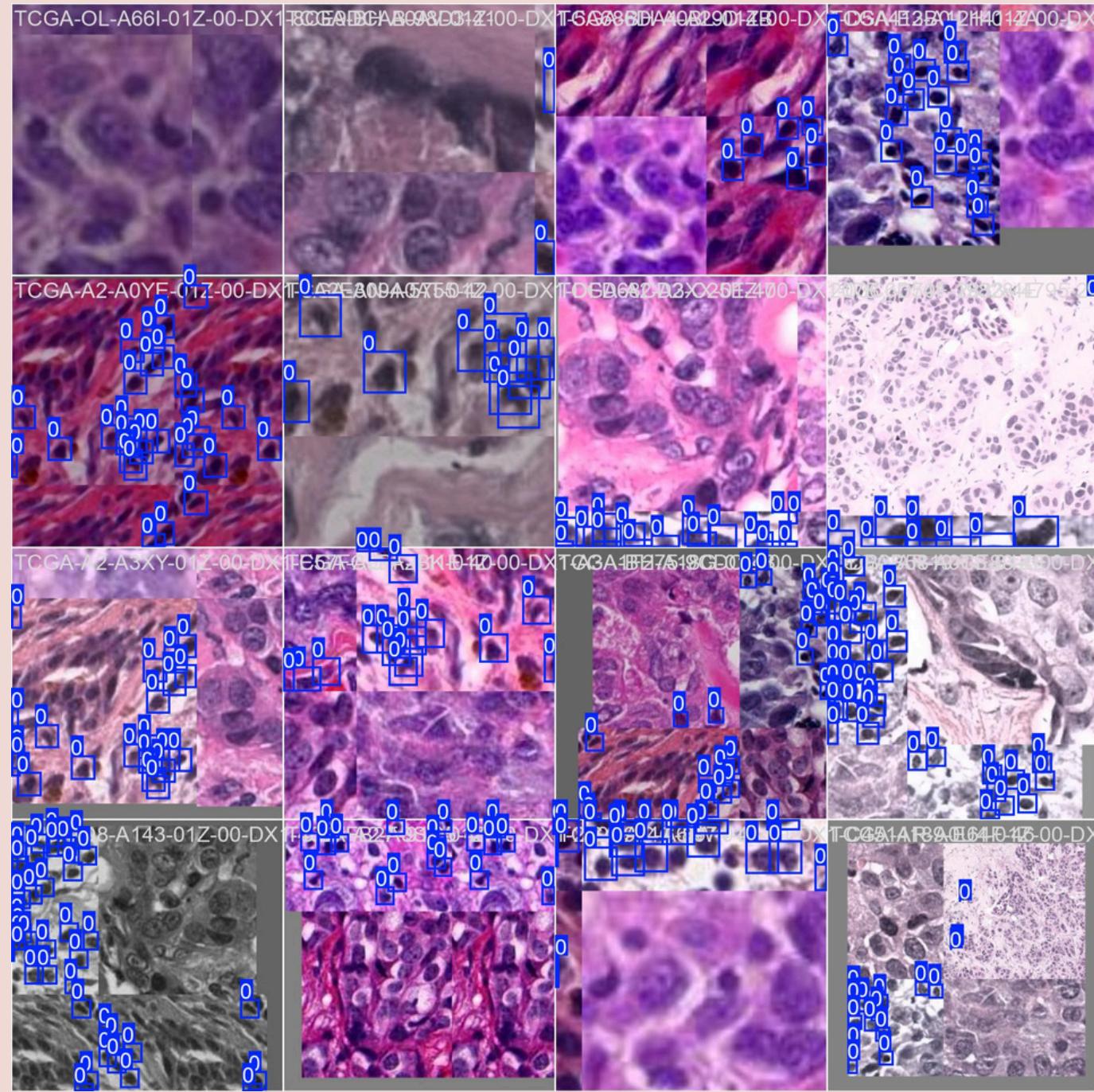
- **Total TIL Area** = Number of TILs × Area of one TIL (in pixels).
- **Stroma Area** = Area of tumor-associated stroma (in pixels).

Developing computer algorithms that can automatically generate a "TIL score" with a high prognostic value.



RESULTS

Detection of Lymphocytes and Plasma Cells

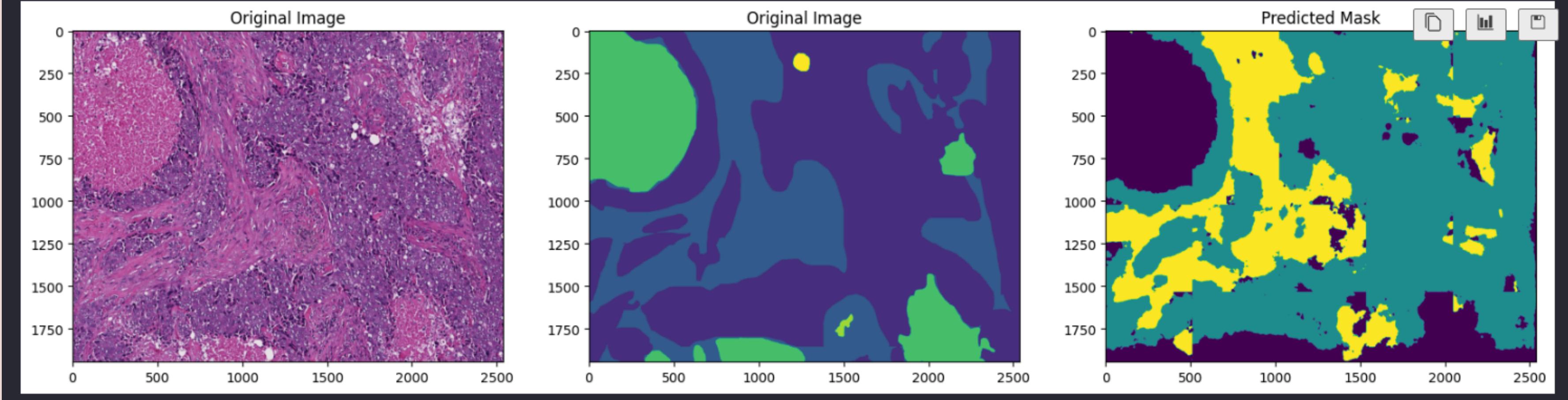


Segmentation of Invasive Tumor and Tumor-Associated Stroma

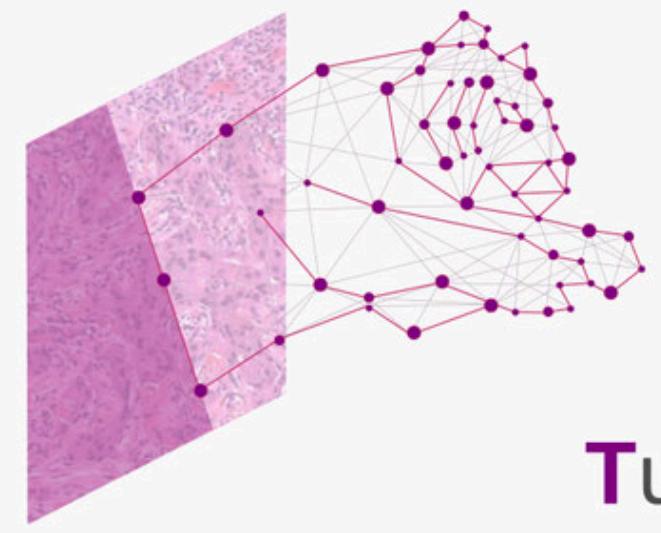
Overall Accuracy: 0.8360

Total No. of pixels misclassified: 859984.0000

Total No. of pixels perfectly classified : 4382896.0000

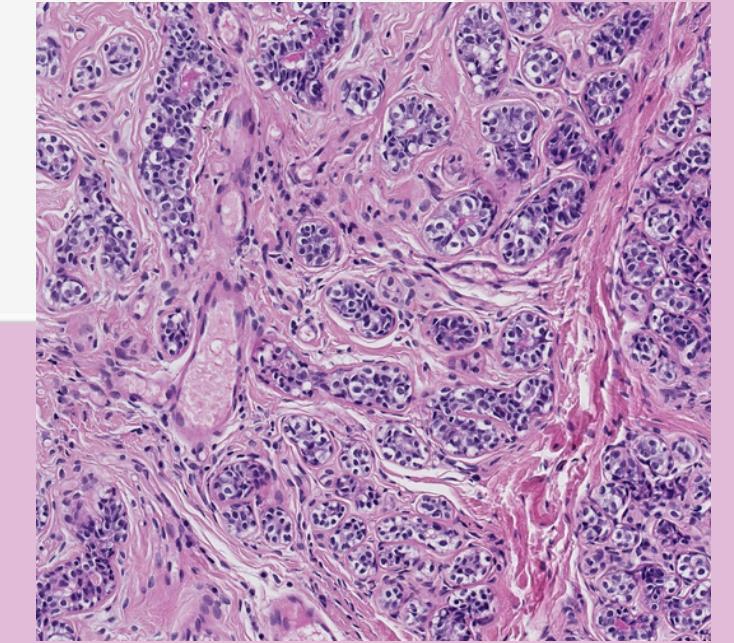


Final IOU Score: 0.4907357394695282
Final F1 Score: 0.6346513628959656



TIGER

Tumor Infiltratin**G** lymphocytes in breast canc**ER**



Prototype Formulation - WiDS'25
Viren Mehta