Automated Identification of Necrotic Regions in Digital Images of Multiplex Immunofluorescence Stained Tissue Using Deep Learning

Anirudh Som[1], Fahime Sheikhzadeh[1], Aïcha BenTaieb[1], Jessica Baumann[2], Mehrnoush Khojasteh[1]

[1]Digital Pathology, Roche Tissue Diagnostics, Santa Clara, California [2]Companion Diagnostics, Roche Tissue Diagnostics, Tucson, Arizona

Background

- **Necrosis:** A spectrum of morphological changes that follow cell death in living tissue, largely resulting from the progressive degradative action of enzymes on the lethally injured cell.
- **Types of necrosis:**

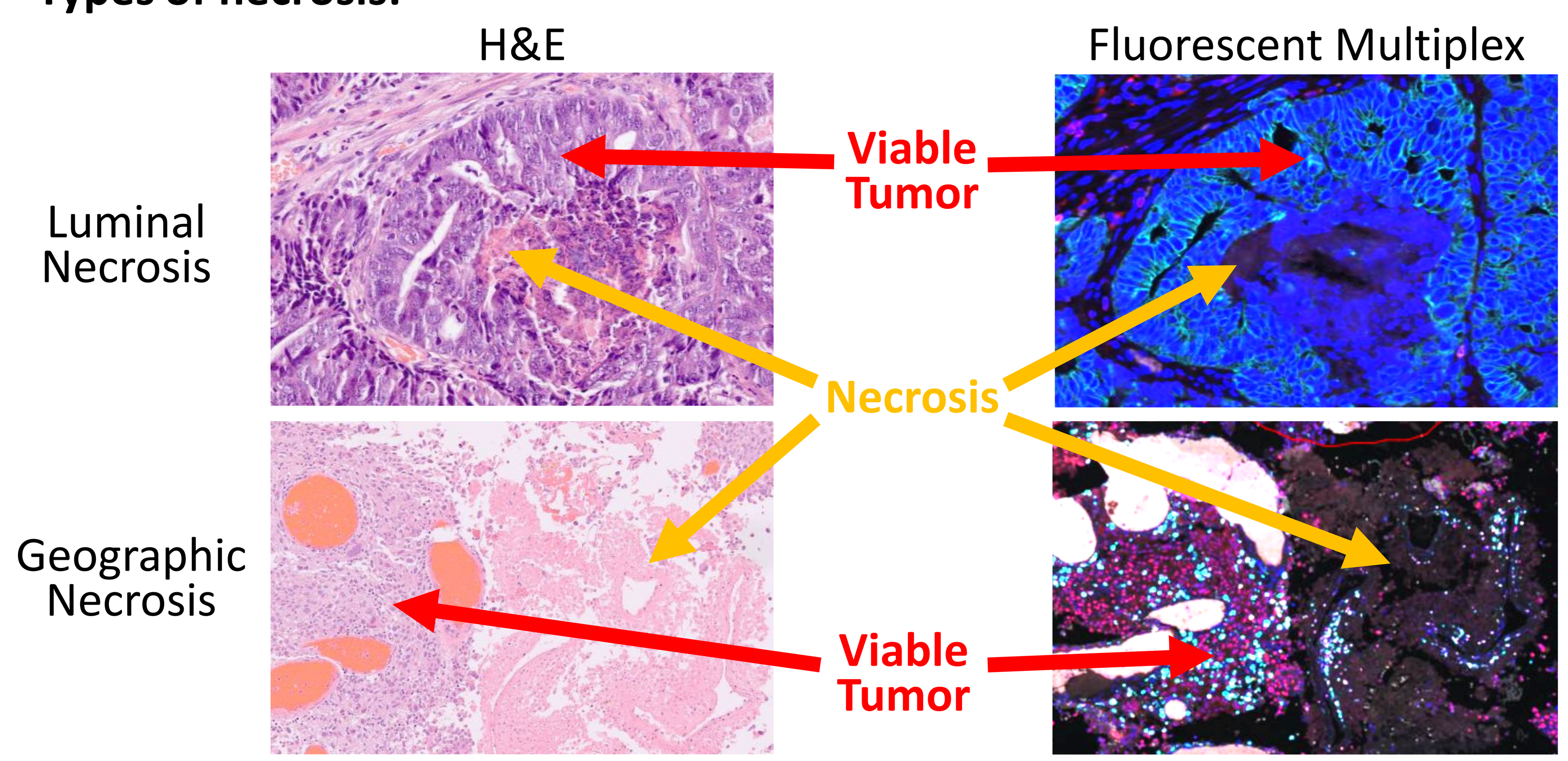

Figure 1: Luminal and geographic necrosis examples in H&E and Fluorescent multiplex stained images.

Necrosis Identification and Challenges

- Excluding necrosis allows us to focus on the Tumor Microenvironment (TME) and get better insight into responses to immunotherapy approaches.
- Manual identification and annotation is the most common practice.

Challenges in manual detection:

- Variation with respect to size, shape, number, region of occurrence.
- Time consuming.
- Reliance on H&E stained image.

Result of manual annotation:

- Expensive process.
- Annotations can vary across pathologists.
- Susceptible to errors and inaccuracies.

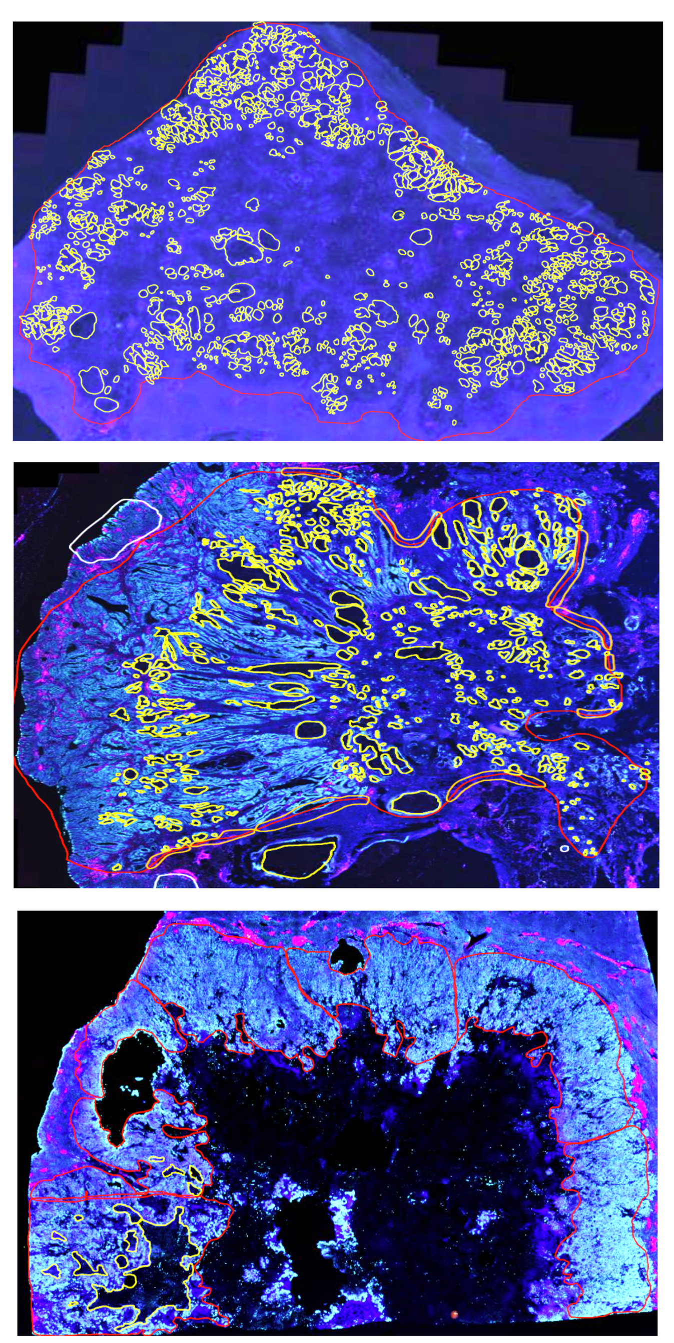

Figure 2: Variation in necrotic regions (yellow) within TME (red).

Methods

Automated Workflow

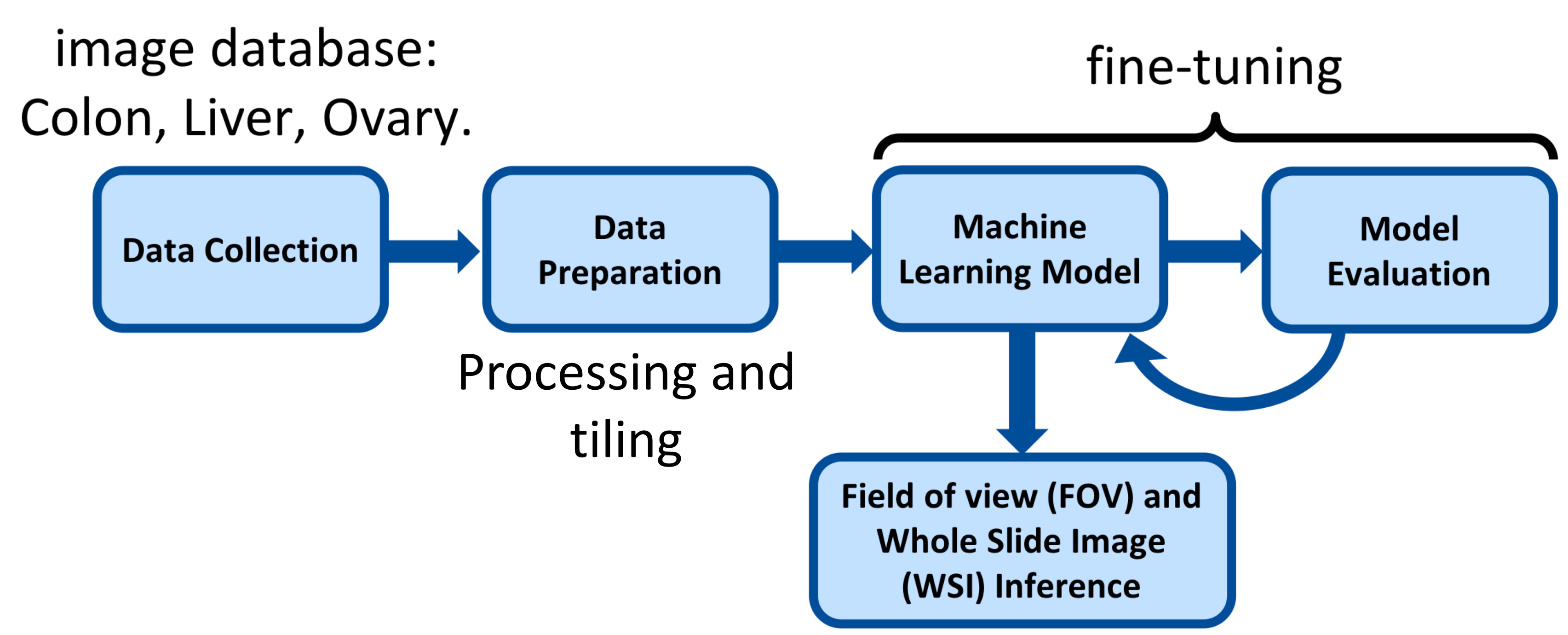

Figure 3: Illustration of workflow for an automated framework.

Gamma Correction

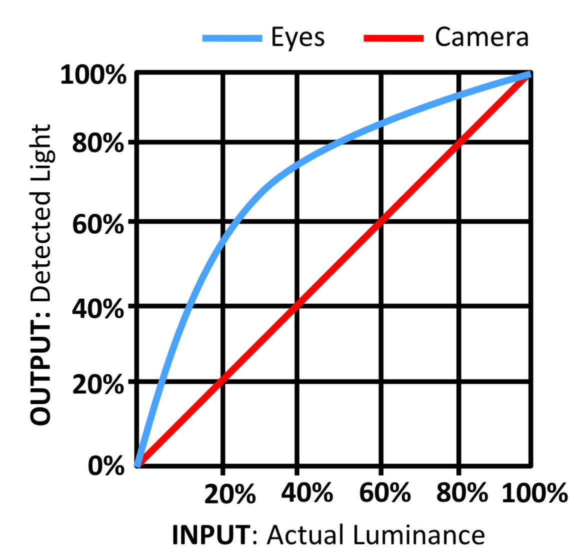

Figure 4: Gamma correction with γ < 1.

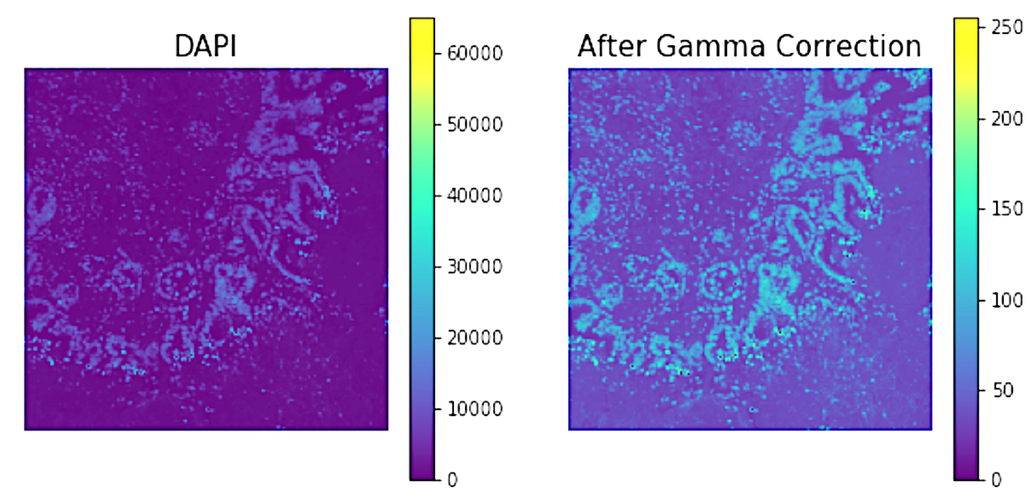

Figure 5: Amplification of lower intensity pixels using gamma correction with γ = 0.5.

U-Net

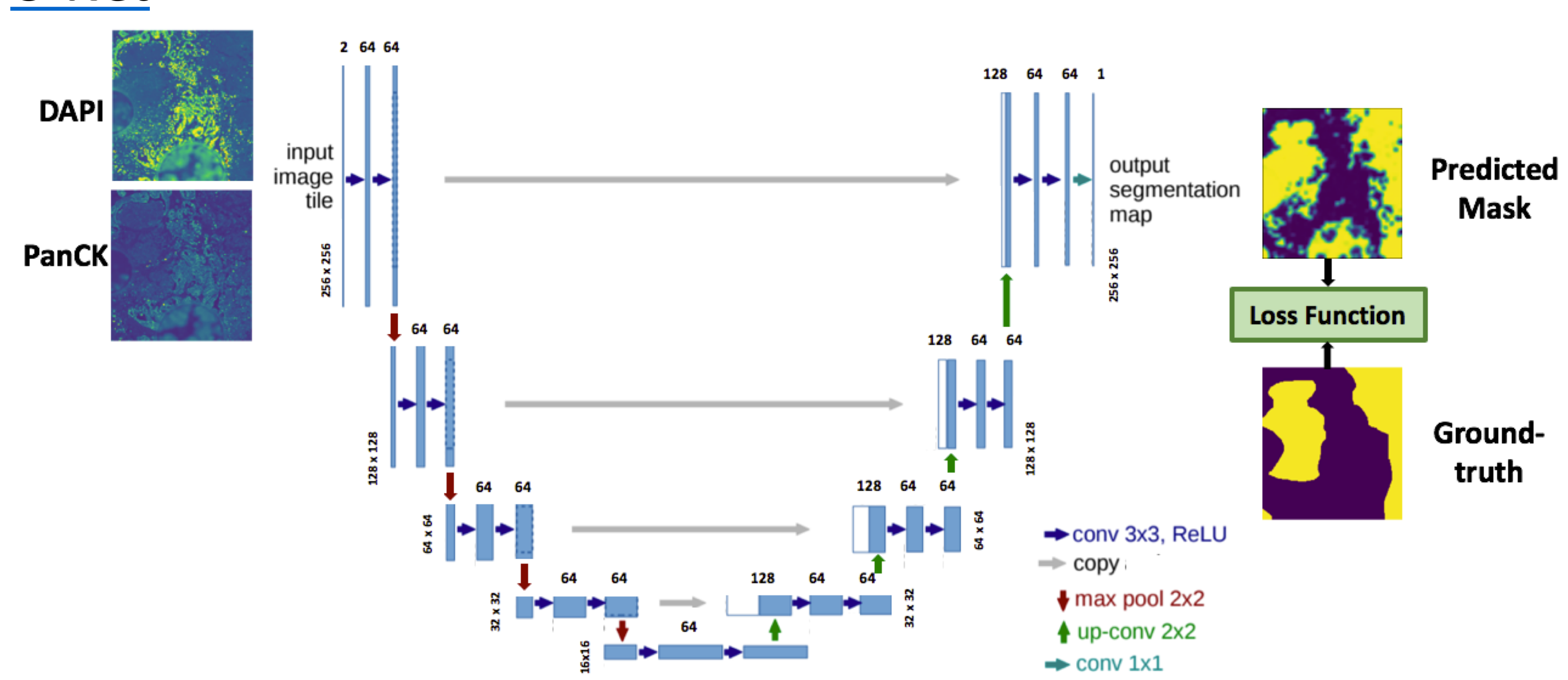

Figure 6: U-Net architecture setup. U-Net is simple, fast to train, gives reasonable results with less amount of training data. U-Net and its variants have achieved state-of-the-art results for medical image segmentation.

Results

- **Loss functions:** Binary cross-entropy, Dice similarity coefficient.
- **Optimizers:** Momentum, Adam.
- **Data augmentation:** Rotation, Translation, Zoom, Shear, Horizontal flip.

Hyperparameters	Dice Similarity
Loss: Binary cross-entropy, **Optimizer:** Momentum, **Learning rate:** 1e-3	**0.82**
Loss: Dice Similarity Coefficient, **Optimizer:** Adam, **Learning rate:** 1e-4	**0.82**

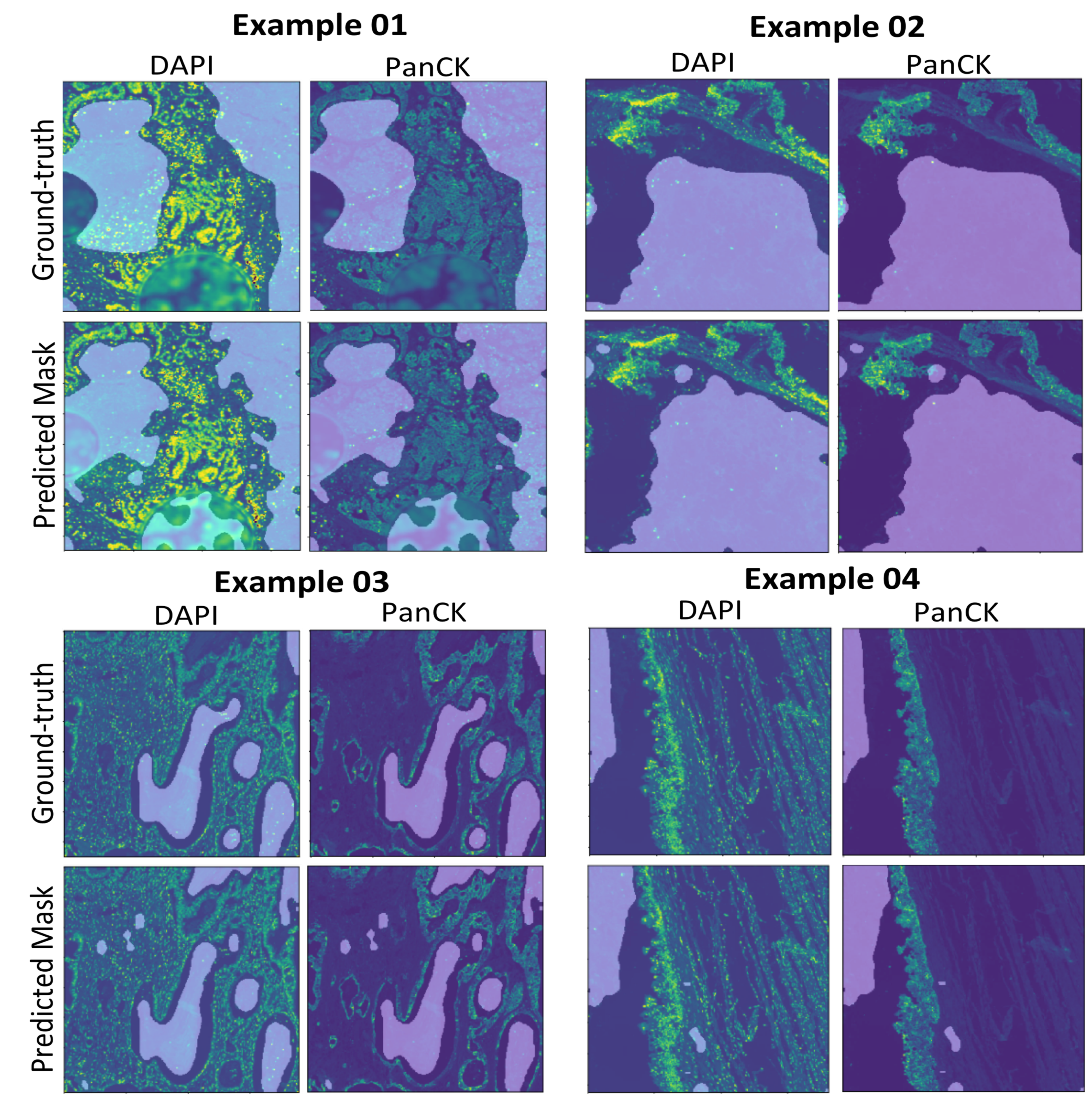

Figure 7: Comparison of ground-truth and predicted masks for different FOVs.

References

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4. Lahiani et al., "Generalising multistain immunohistochemistry tissue segmentation using end-to-end colour deconvolution deep neural networks", IET Image Processing, 2019.