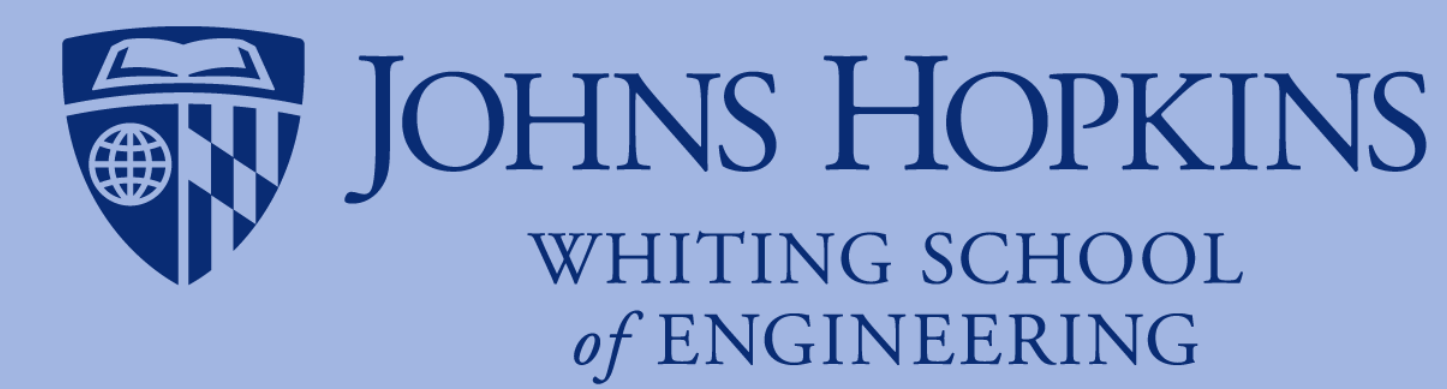


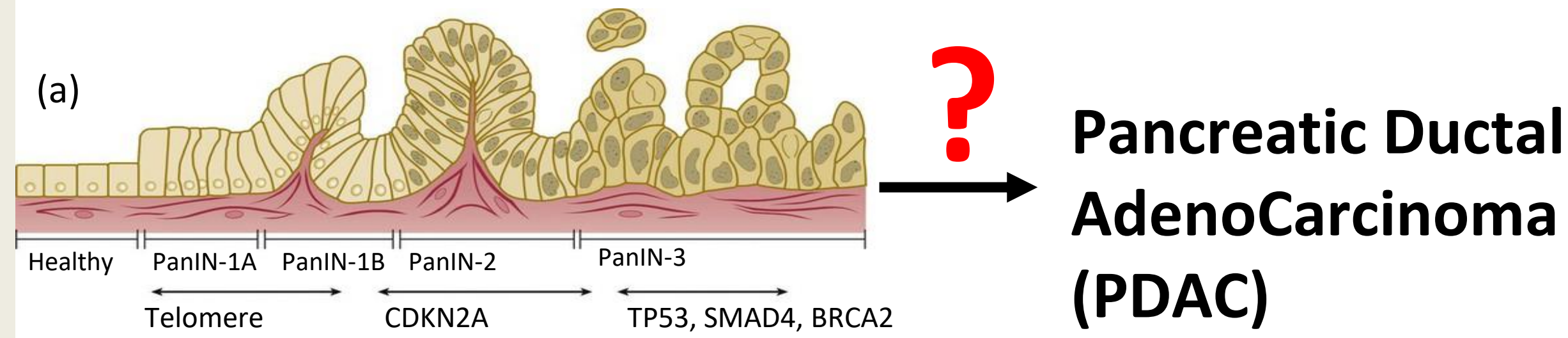
# Characterization of the 3D microanatomy of the pancreas and pancreatic cancer *in situ* at single cell resolution

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## Development of pancreatic cancer from precursor lesions



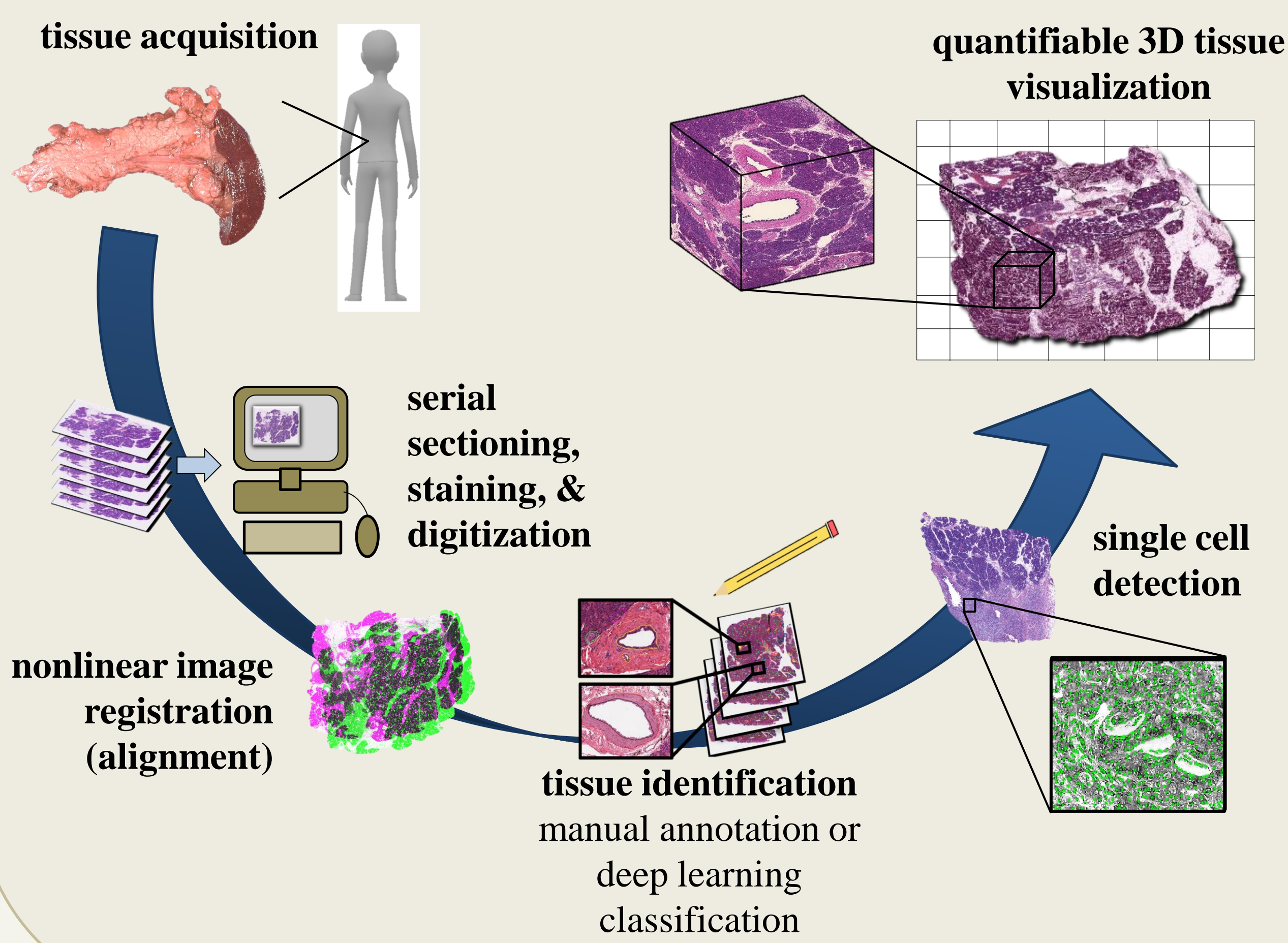
### Pancreatic Intraepithelial Neoplasia (PanIN)

- Mucinous, elongated epithelium within pancreatic ducts
- Asymptomatic precursor to PDAC

### Pancreatic Ductal AdenoCarcinoma (PDAC)

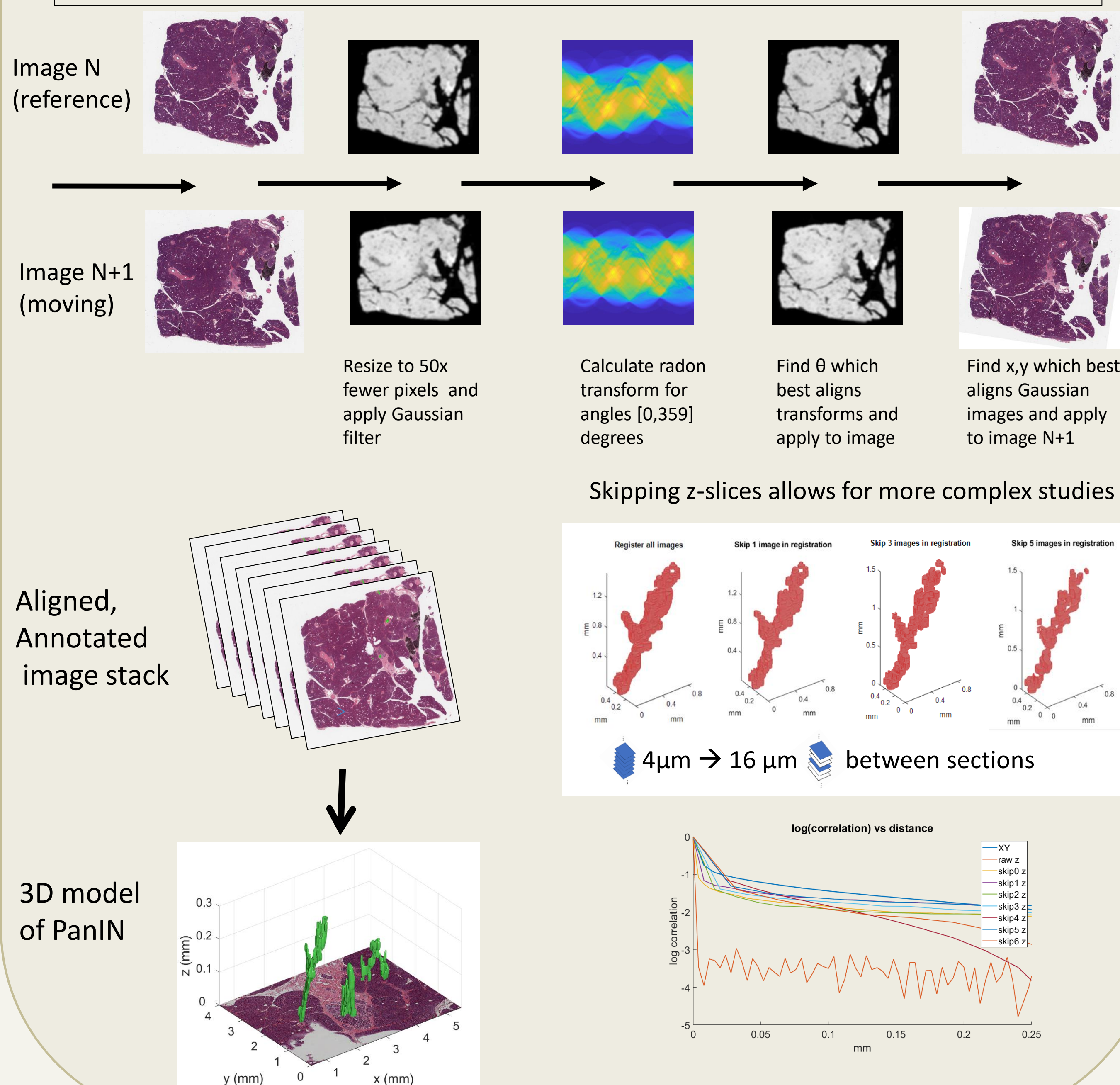
- Typically diagnosed at distant stage
- 8% 5-year survival rate<sup>(2)</sup>

## 3D reconstruction of serially sectioned human pancreas

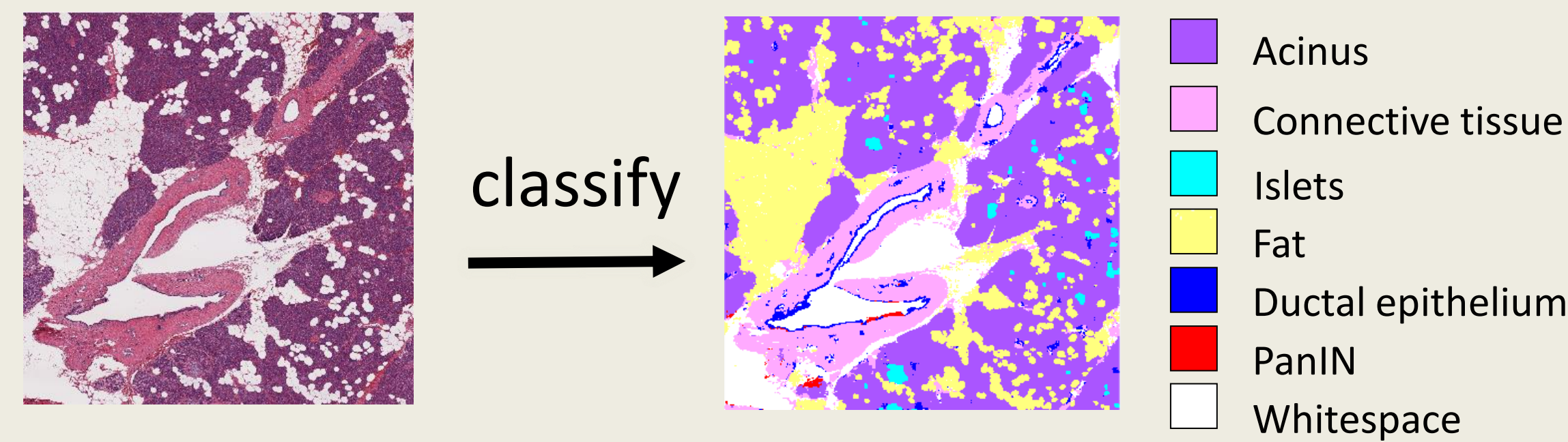


## Registration aligns images into digital volume

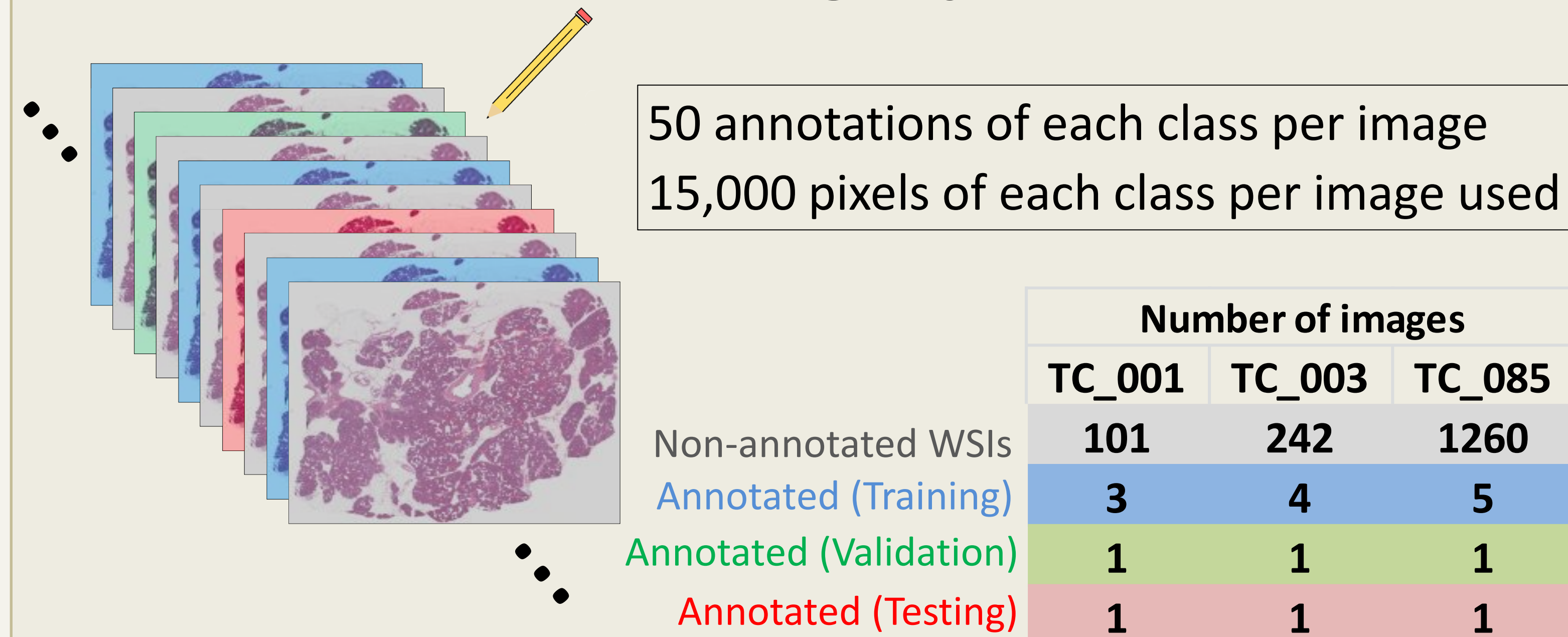
Input: stack of 101 sliced H&E stained images each 4μm thick  
 1. Global (course) registration: corrects whole tissue misalignment in angle and position  
 2. Local (fine) registration: corrects tissue stretching & folding by registering areas of interest  
 Output: registered images and 3D PanIN model  
 Computational time: 25 minutes



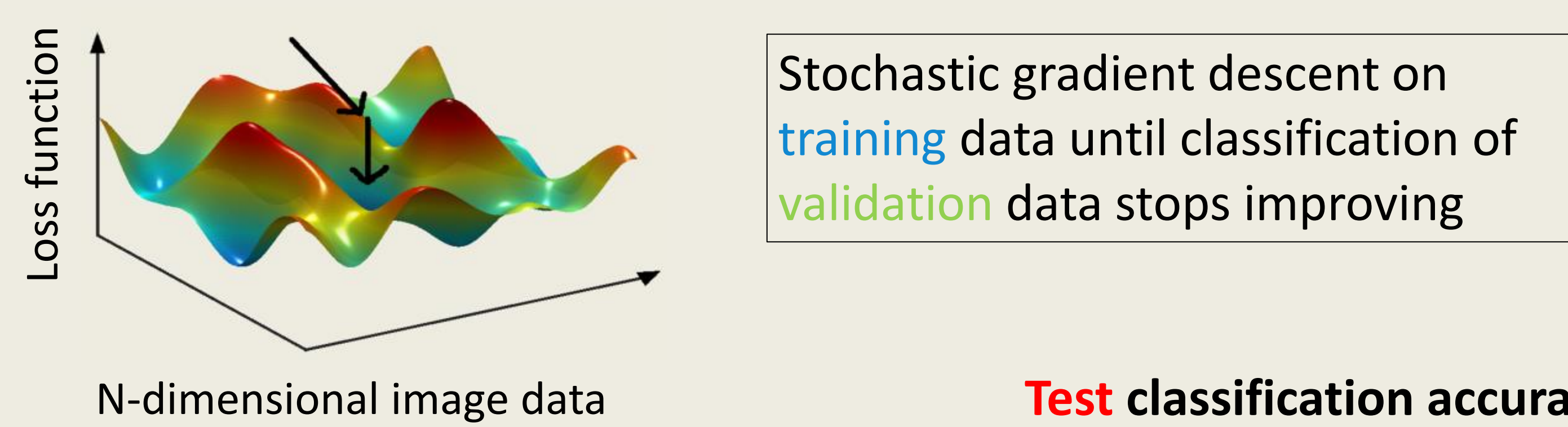
## Deep learning labels eight distinct tissue types using H&E stain



### 1. Annotate tissue images from block



### 2. Train and validate semantic segmentation network



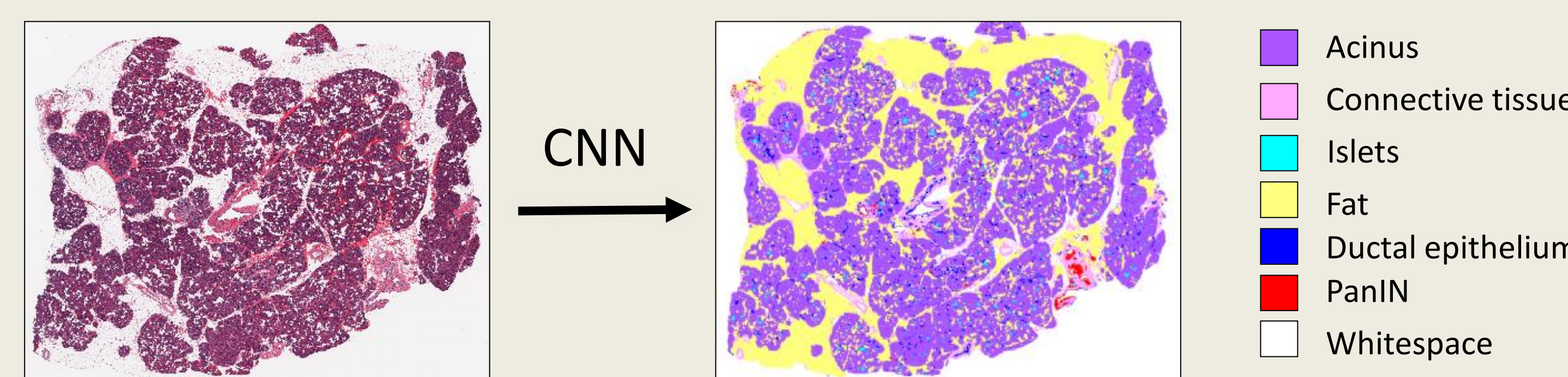
Sample Input: 95x95x3 Gaussian sampled image

Output: calculated tissue type of center pixel

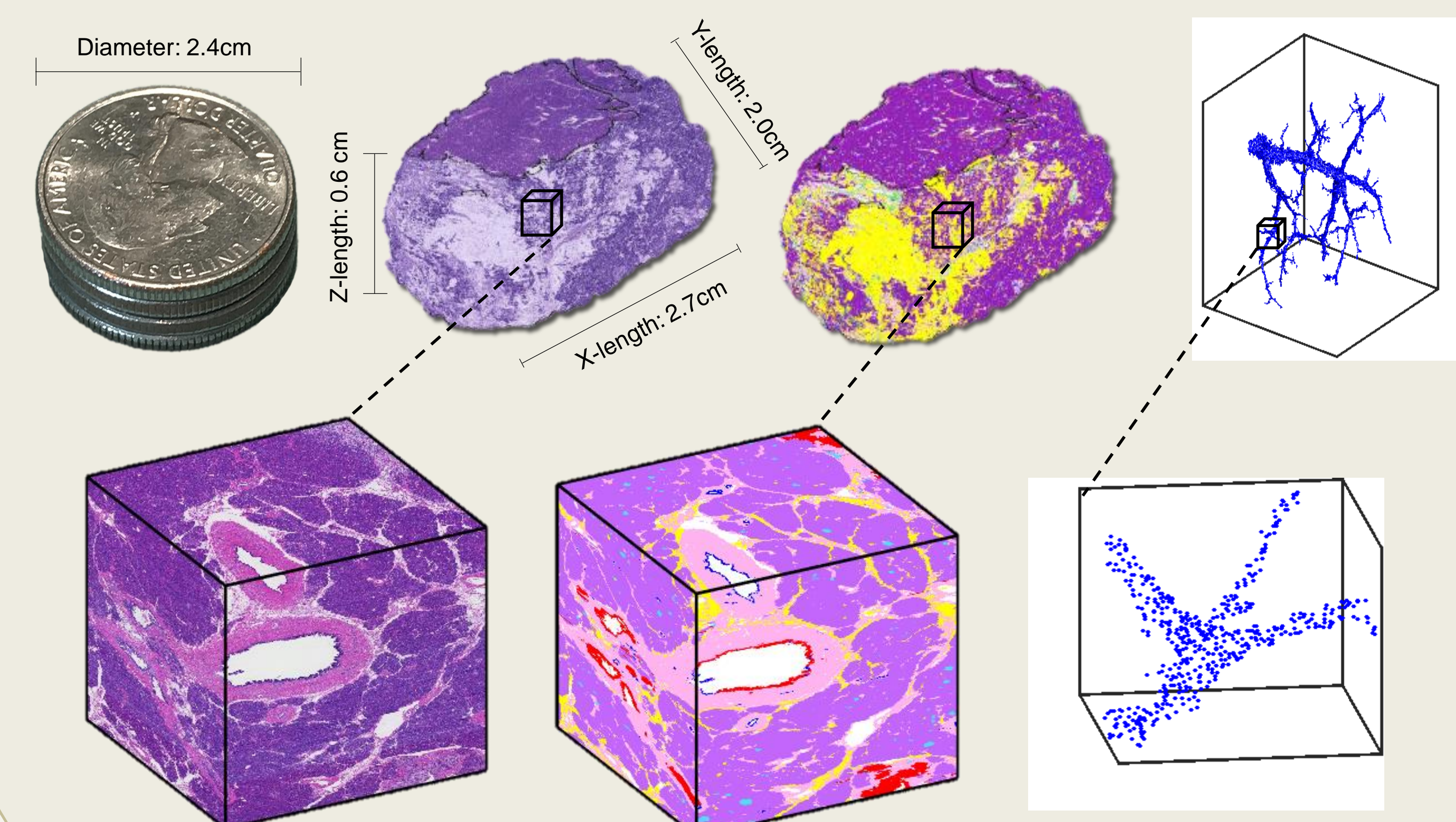
### Test classification accuracy

Islet	96.30%
Ductal Epithelium	99.50%
Blood vessel	92.40%
Fat	96.00%
Acinus	98.80%
Connective Tissue	96.90%
PanIN	85.40%
Non-tissue	98.10%

### 3. Classify non-annotated images in block

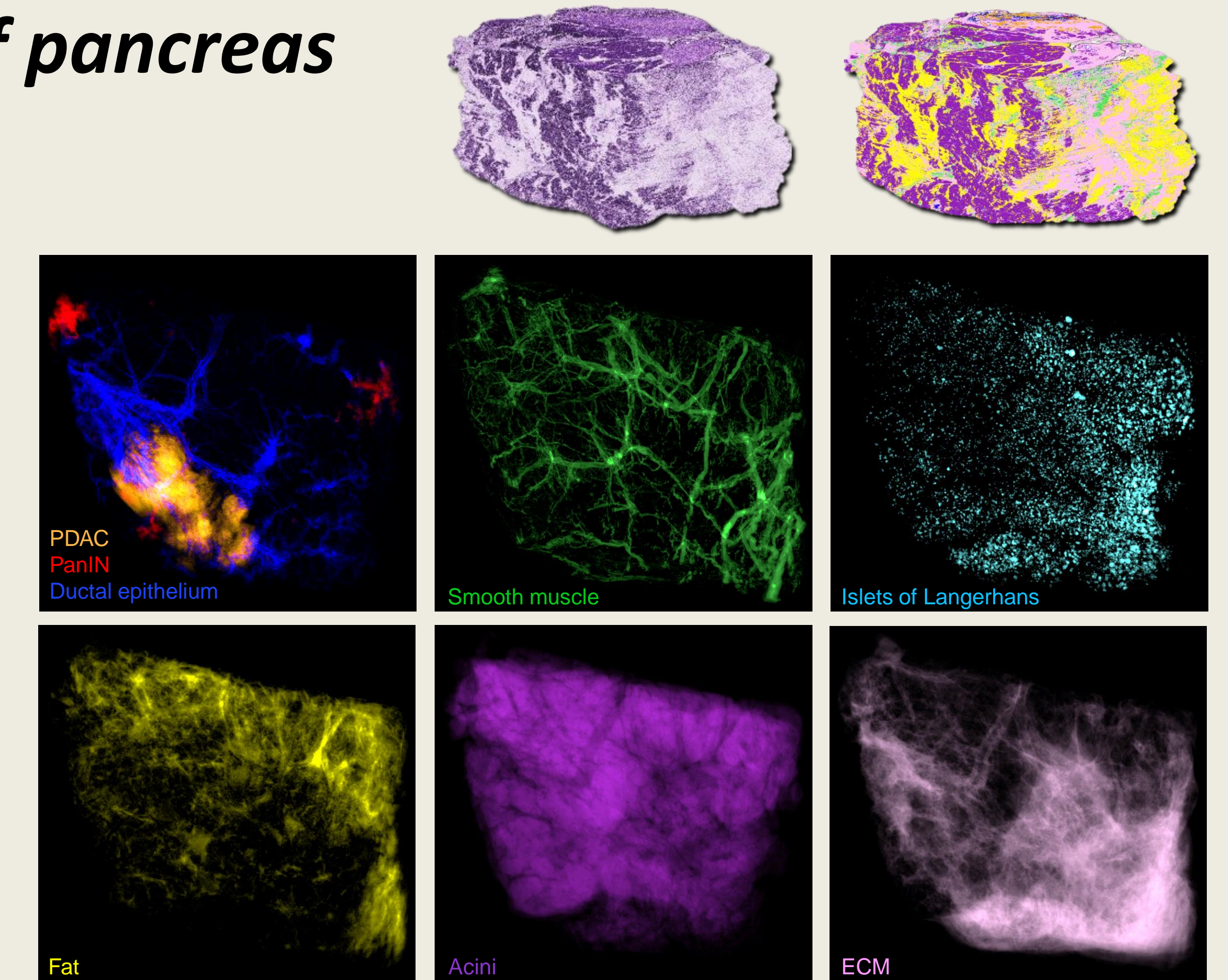


### 4. Build tissue volume from classified images

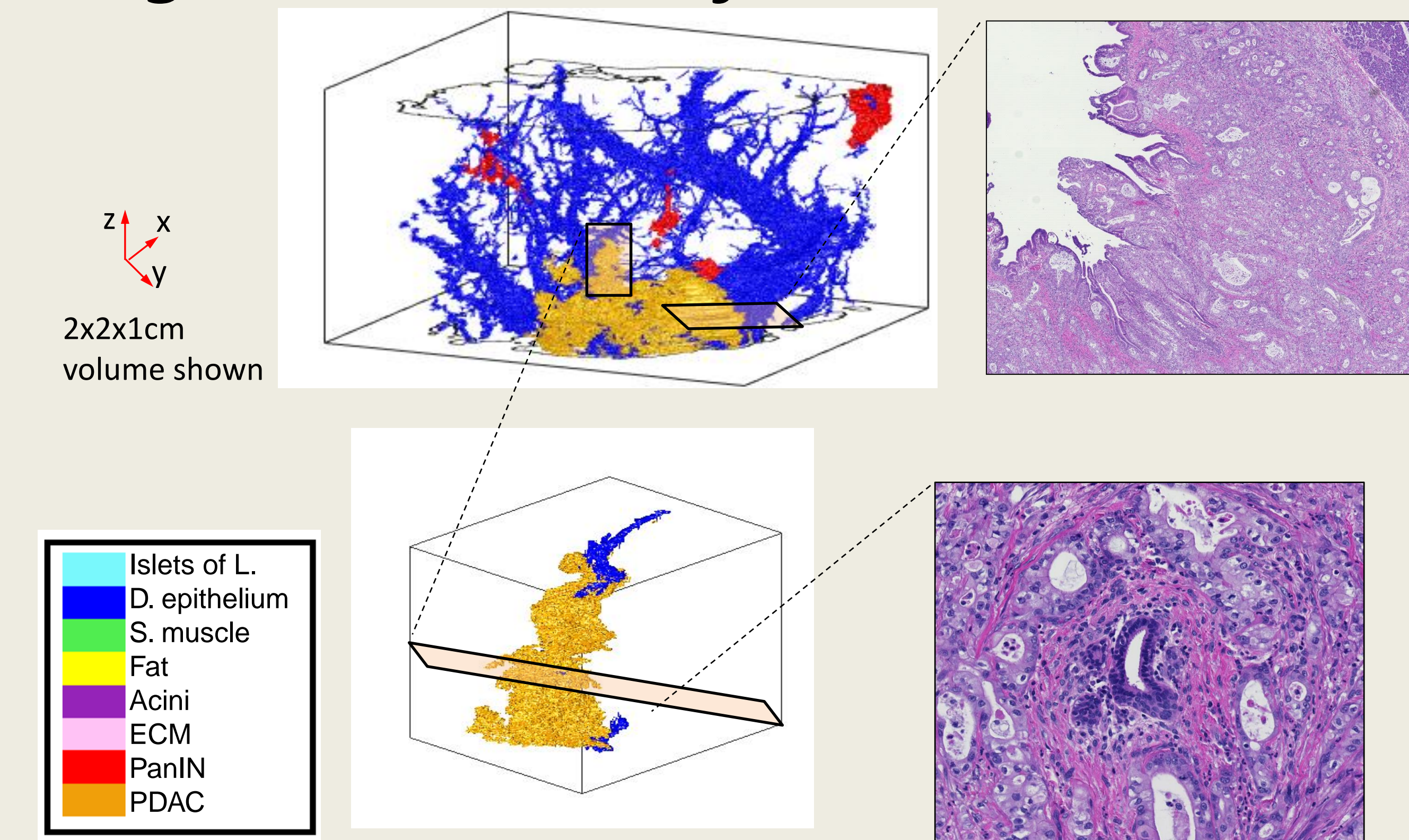


## 3D microanatomy of the cancerous pancreas

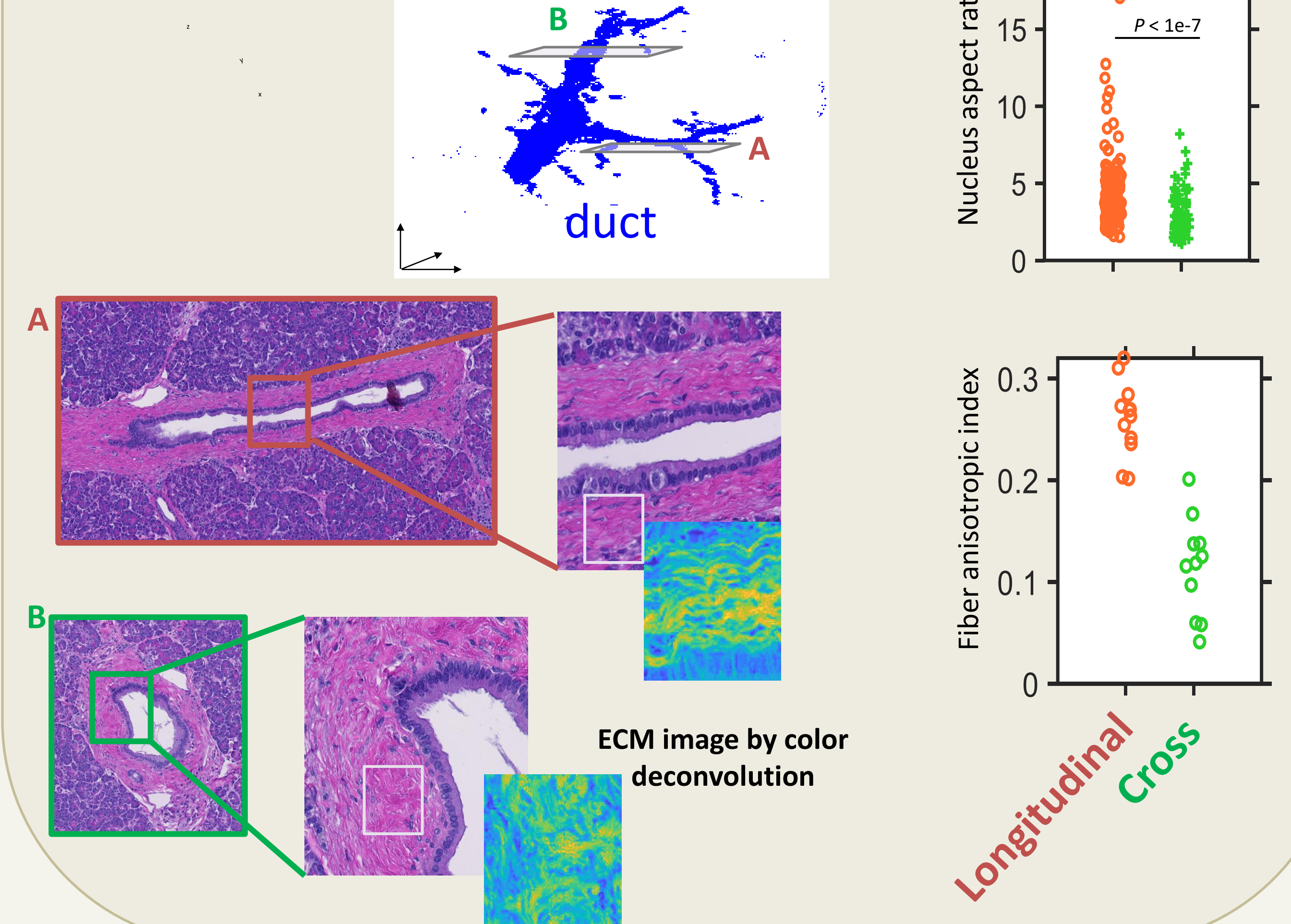
Z-projections convey 3D heterogeneity of pancreas



Pancreatic ductal submucosa aligns along the direction of the duct



Longitudinal view  
Cross view



## References

- (1) Zhu, Liqin, et al. "Acinar cells contribute to the molecular heterogeneity of pancreatic intraepithelial neoplasia." *The American journal of pathology* 171.1 (2007): 263-273.
  - (2) Siegel, Rebecca L., Kimberly D. Miller, and Ahmedin Jemal. "Cancer statistics, 2018." *CA: a cancer journal for clinicians* 68.1 (2018): 7-30.
  - (3) Mehta, Kapil, and Amy Han. "Tissue transglutaminase (TG2)-induced inflammation in initiation, progression, and pathogenesis of pancreatic cancer." *Cancers* 3.1 (2011): 897-912.
  - (4) Rebour, Vinciane, et al. "Obesity and fatty pancreatic infiltration are risk factors for pancreatic precancerous lesions (PanIN)." *Clinical Cancer Research* 21.15 (2015): 3522-3528.
- (a) Photo Credit: <https://clinicalgate.com/carcinoma-of-the-pancreas-2/>