Analysis of 3D pathology samples using weakly-supervised AI

Andrew H. Song, Mane Williams, Drew F.K. Williamson, Sarah S.L. Chow, Guillaume Jaume, Gan Gao, …, Jonathan T.C. Liu*, Faisal Mahmood*

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asong@bwh.harvard.edu, jonliu@uw.edu, faisal.mahmood@bwh.harvard.edu

Mass General Brigham · Harvard Medical School · Mahmood Lab, AI for Pathology · University of Washington

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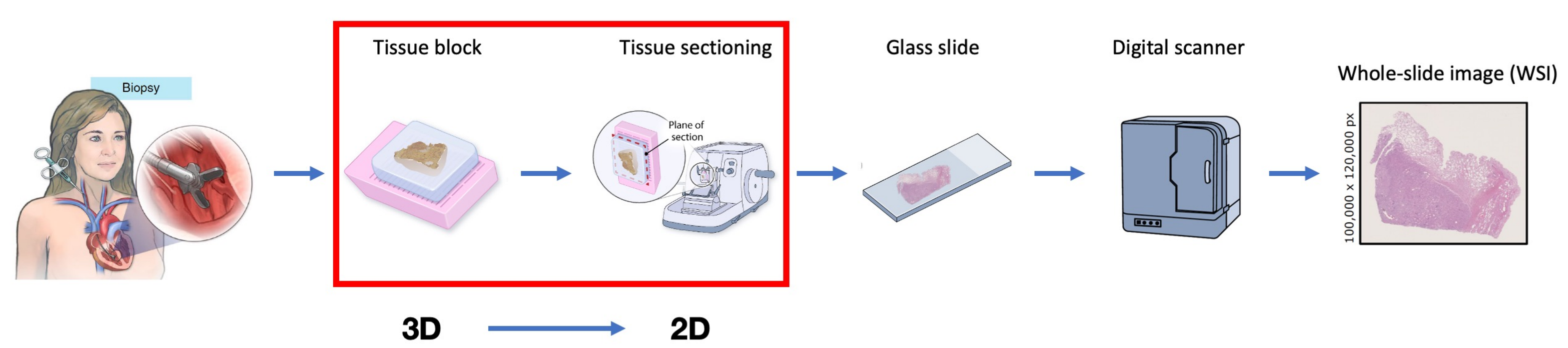
Motivation

Human tissue is inherently 3D!



- However, the current clinical/computational practice entirely focuses on *thinly-sliced 2D tissue sections* [1,2]. This leads to

⇒ **Sampling bias and misdiagnosis** due to heterogeneous tissue volume

⇒ **Mischaracterization of 3D morphological structure** [3]

3D pathology paradigm can address these limitations!

The current state of 3D pathology

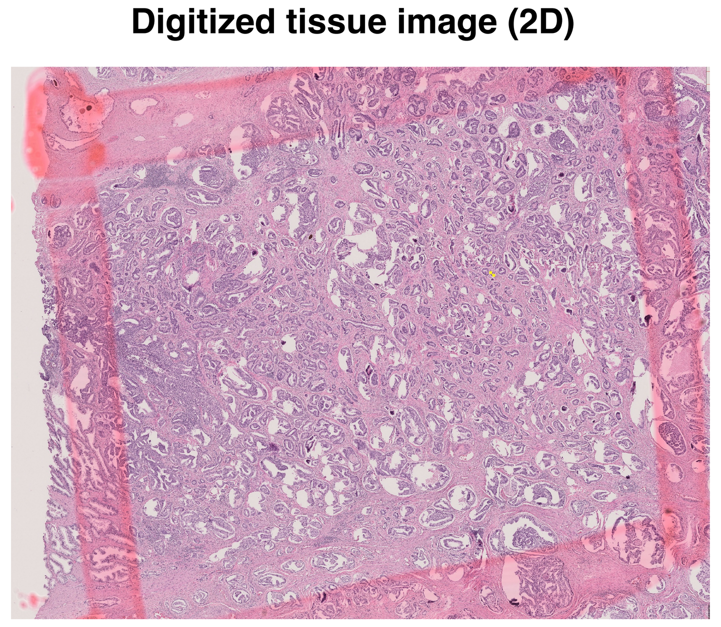
3D pathology requires innovations in hardware and software

High-resolution 3D imaging modalities (hardware)

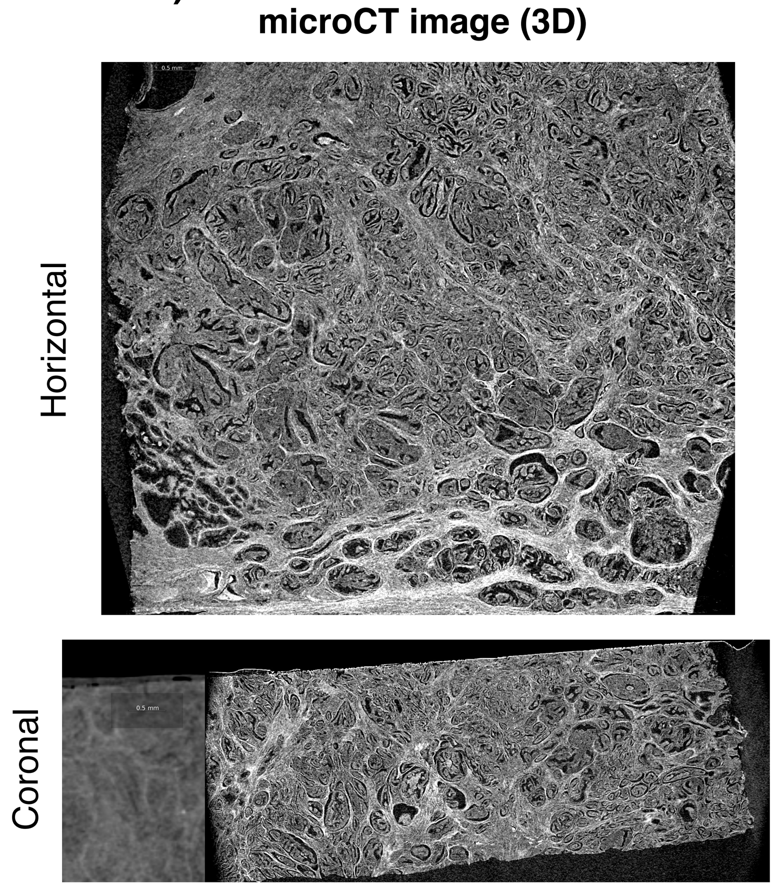
Serial sectioning & registration | **microCT** | **Open-top light-sheet microscopy [4]**

Examples of 3D pathology image (Prostate cancer)

Digitized tissue image (2D)

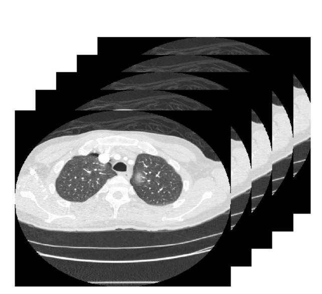


microCT image (3D)



No computational pipeline to process volumetric data exists!

3D radiology

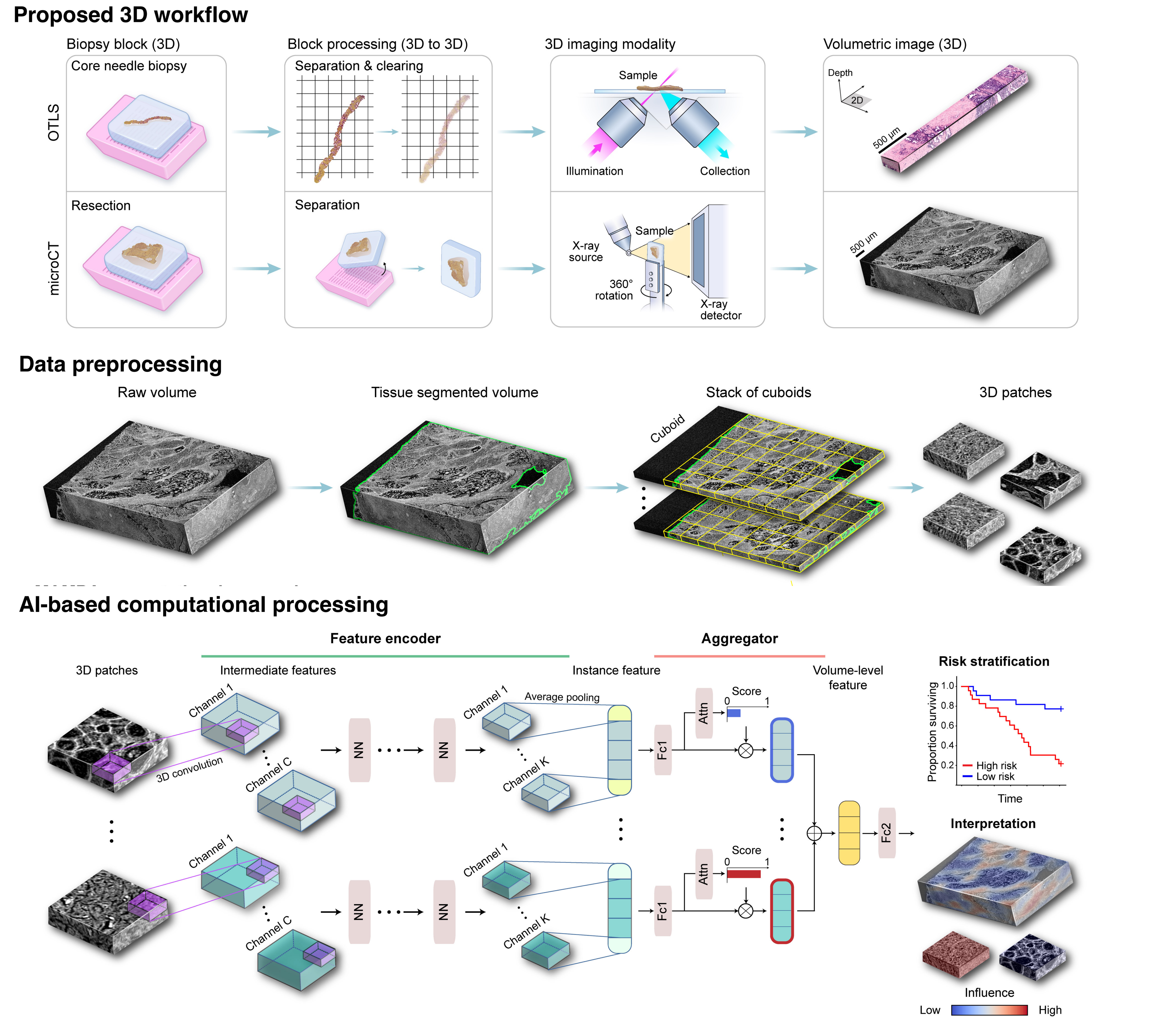


- **Size: Mega**-voxel
- **Res.:** 1~2 mm /voxel

3D pathology

- **Size: Giga ~ Tera**-voxel
- **Res.:** 0.5~4 μm /voxel

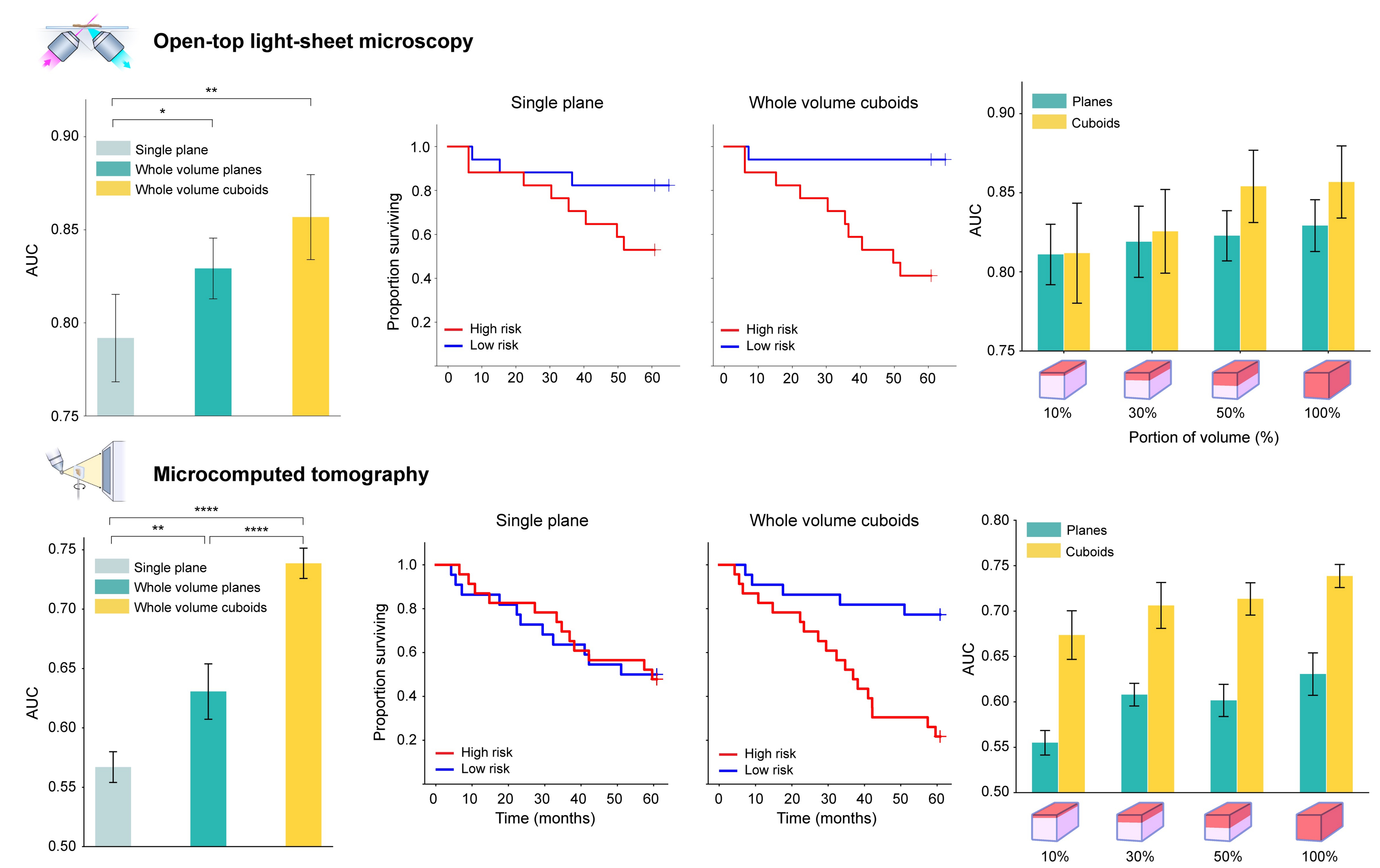
TriPath: 3D computational pathology toolbox



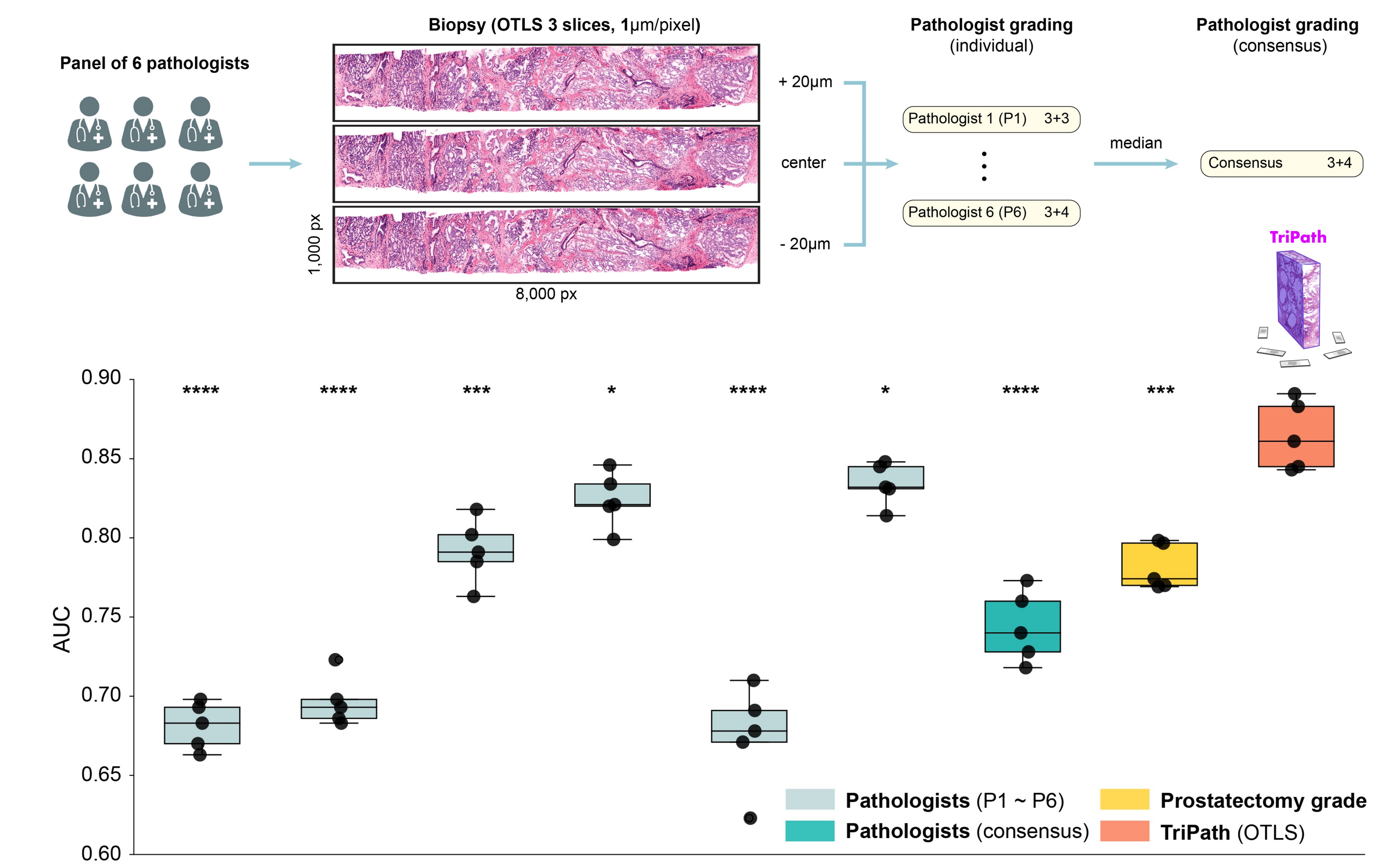
Multiple instance learning (weakly-supervised learning) in 3D

Risk stratification in Prostate cancer

Prostate cancer recurrence risk stratification (high-risk vs. low-risk)



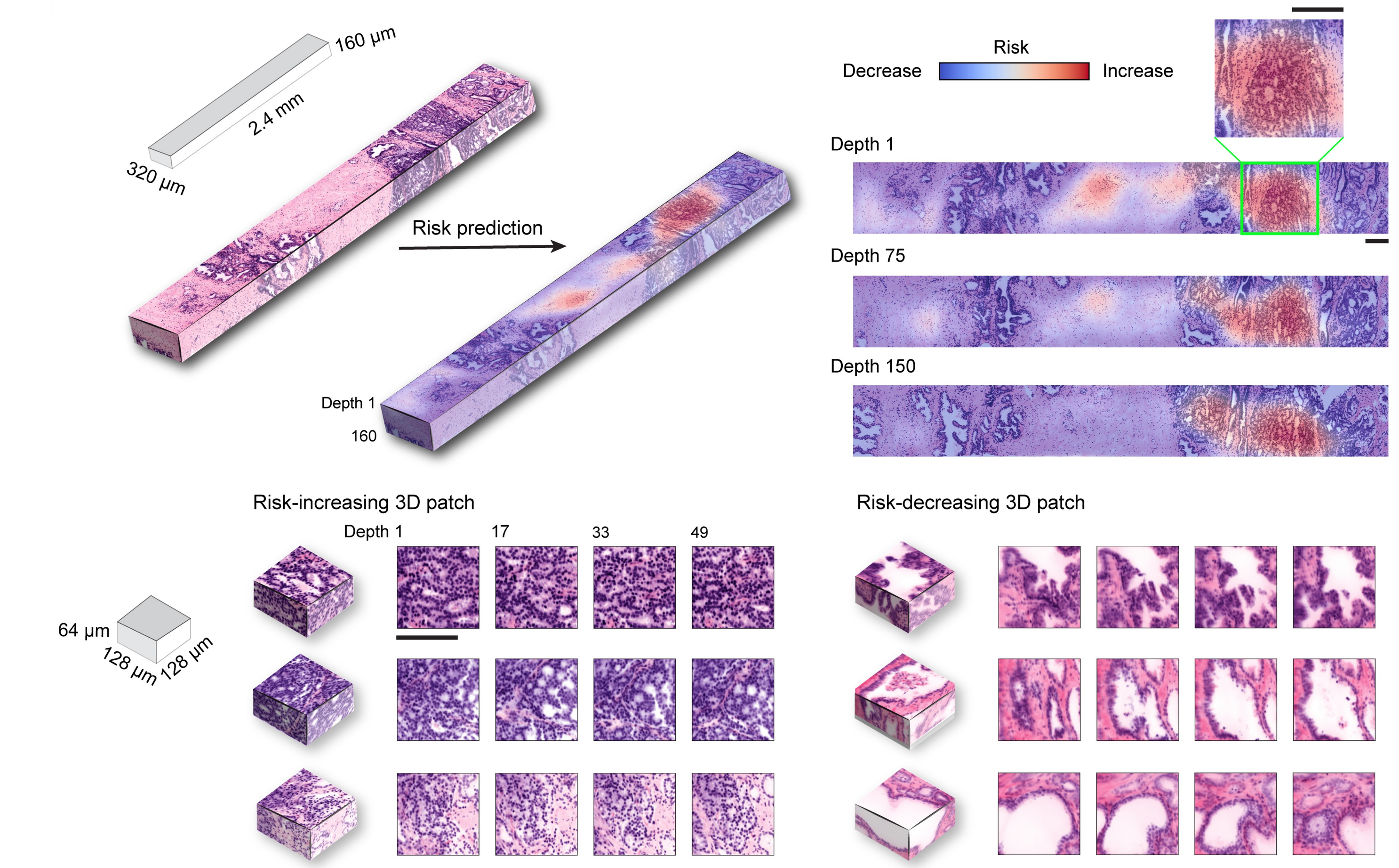
Clinical validation



Reader study with six board-certified pathologists

⇒ TriPath outperforms all clinical baselines, demonstrating clinical potential

TriPath for Interpretability



Risk heatmap captures well-known prognostic biomarkers

⇒ Identifies risk-increasing/decreasing 3D patches automatically

⇒ With larger validation cohort, novel 3D biomarker discovery possible

References

- [1] Song AH et al., Analysis of 3D pathology samples using weakly-supervised AI. *Cell*, 2024
- [2] Song AH et al., Artificial intelligence for digital and computational pathology. *Nature Reviews Bioengineering*, 2023
- [3] Liu JTC et al., Harnessing non-destructive 3D pathology, *Nature Biomedical Engineering*, 2021
- [4] Bishop K et al., An end-to-end workflow for nondestructive 3D pathology, *Nature Protocols*, 2024

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