

Z-Stack Scanning can Improve AI Detection of Mitosis: A Case Study of Meningiomas

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Introduction

- Z-Stack scanning** is multi-planar digital pathology technique that captures **multiple focal planes** alongside the **z-axis** of a glass slide.
- Capture with multiple focal depth, but bring larger file size and longer scanning time.
- Whether **z-stack** can enhance pathology analysis is **debatable** due to **a lack of standardized environment with quantitative evaluation**.

Contribution

- First **quantitative** evidence showing Z-stacked whole slide images **significantly improve deep learning mitosis detection sensitivity** by **17.14%** against traditional single-layer scans, based on the same set of glass slides scanned by three scanners across three different vendors.

Materials and Methods

Specimen collection and Annotation:

- Selected **22** Hematoxylin and Eosin (H&E) **meningioma** glass slides and scanned with **3DHISTECH Panoramic 250 scanner**, 41X objective, z-stack (five layers, 0.6μm gap) setting.
- Three pathology professionals annotated **6,350** mitoses inside digital scans.

Deep Learning Pipeline Training:

- Mitosis detection pipeline consists of **a segmentation model** (PSPNet OR Segformer OR DeepLabV3+) and **four CNNs** (EfficientNet -b3, -b5, EfficientNetv2 -s, -m).
- Trained based on a **cross-center cohort** of public (MIDOG++ [1], MITOS_WSI_CMC [2], MITOS_WSI_CCMCT [3]) and in-house datasets from UCLA [4].

Testing Procedure:

- Scan** the same 22 slides in both **Z-stack** and **single-layer** settings by **three scanners**: (1) 3DHISTECH Panoramic 480DX, (2) Leica GT 450, and (3) Zeiss AxioScan 7.
- Compare **precision** and **sensitivity** of the deep learning pipeline.

Result Summary

Slide Size:

- Single layer: 87.02GB
- Z-Stacking: 418.92GB (five layers, +381%)

Deep Learning Performance:

- Significant** improvement in **sensitivity** (average: **+17.14%**, min: +6.23%, max: +39.24%).
- Marginal** impact in the **precision** (average: +0.53%, min: -7.86%, max: +9.70%).
- Overall F1 performance was improved.

Future Directions:

- Compress multiple z-stacked layers into a single layer (i.e., extended focus) to reduce file size and compare deep learning performance.
- Extend experiments to other small-scaled histopathological patterns (e.g., Helicobacter pylori).

Figures and Results

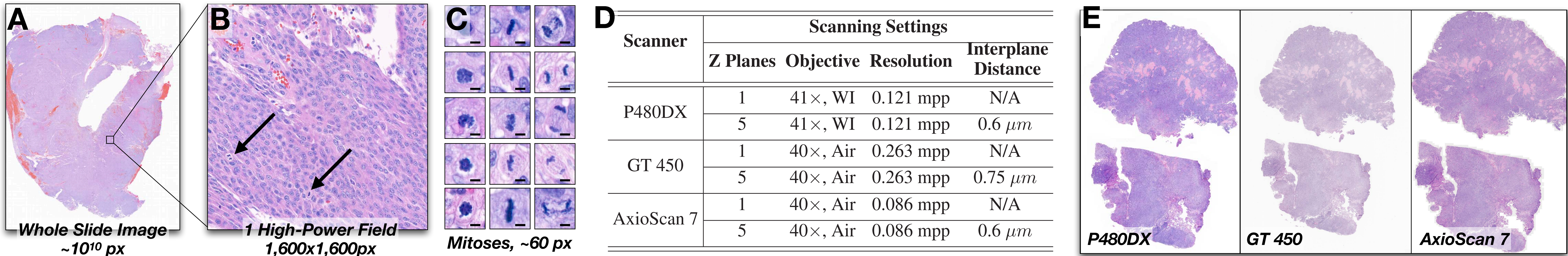


Figure 1 (A) A typical pathology whole slide image (WSI) scanned at 40X magnification has ~10¹⁰ pixels. (B) A high-power field (HPF) has about 1,600x1,600 pixels (WHO CNS 5: 1HP-F=0.16mm², 0.25 μm / pixel). (C) Mitoses are small sized (~60 pixels or 15μm) histopathological features, bar=5μm. (D) Settings used for single-layer and z-stack scanning, mpp: μm per pixel, WI: water immersion. (E) Thumbnails WSIs from a glass slide digitalized by three scanners.

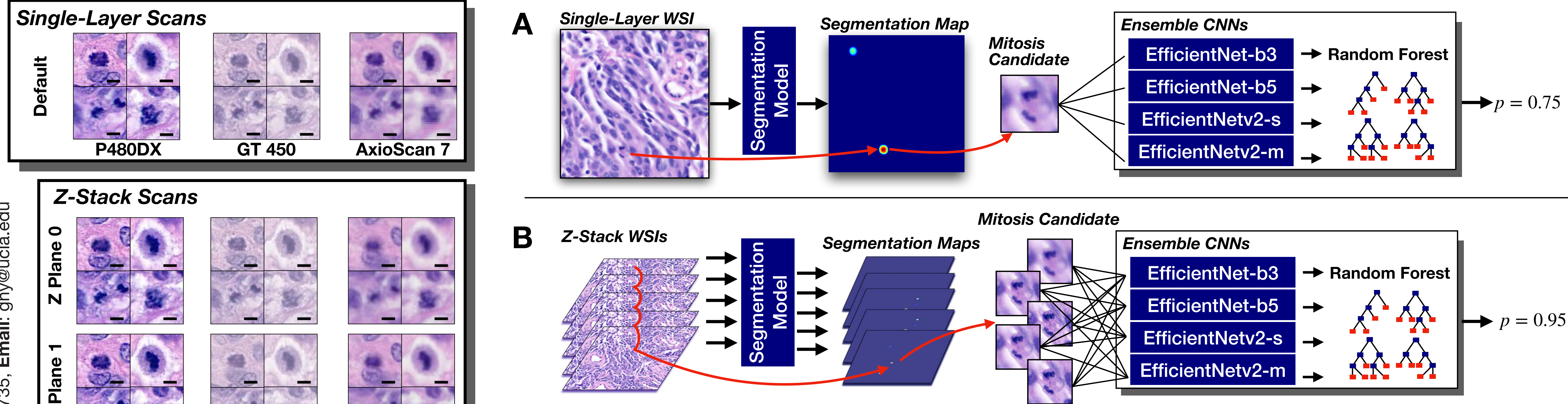


Figure 3 Deep learning mitosis detection pipeline for (A) single-layer WSIs and (B) z-stacked WSIs.

A					
Scanner	Segmentation	Single-Layer	Z-Stack	Δ	p
P480DX	PSPNet	0.633	0.726	+14.74%	<0.001
	Segformer	0.664	0.726	+9.32%	<0.001
	DeepLabV3+	0.675	0.717	+6.23%	<0.001
GT 450	PSPNet	0.636	0.739	+16.33%	<0.001
	Segformer	0.616	0.740	+20.09%	<0.001
	DeepLabV3+	0.681	0.773	+13.52%	<0.001
AxioScan 7	PSPNet	0.398	0.554	+39.24%	<0.001
	Segformer	0.447	0.574	+28.28%	<0.001
	DeepLabV3+	0.583	0.713	+22.25%	<0.001
Average		0.601	0.704	+17.14%	N/A

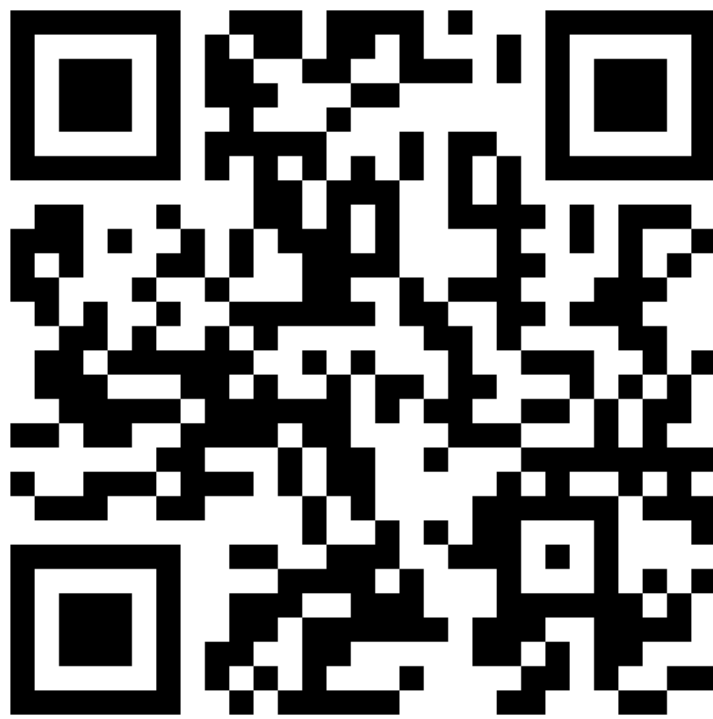
B					
Scanner	Segmentation	Single-Layer	Z-Stack	Δ	p
P480DX	PSPNet	0.768	0.787	+2.46%	0.999
	Segformer	0.763	0.793	+3.91%	<0.001
	DeepLabV3+	0.720	0.790	+9.70%	<0.001
GT 450	PSPNet	0.714	0.735	+3.04%	0.957
	Segformer	0.770	0.710	-7.86%	<0.001
	DeepLabV3+	0.729	0.704	-3.46%	0.825
AxioScan 7	PSPNet	0.815	0.802	-1.59%	0.999
	Segformer	0.845	0.834	-1.31%	0.999
	DeepLabV3+	0.739	0.729	-1.30%	0.999
Average		0.753	0.757	+0.53%	N/A

Figure 4 (A) Sensitivity/recall and (B) Precision of three deep learning pipelines on WSIs from three scanners

Check out our pre-print (QR Code) for more information!

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