CO-PILOT: Dynamic Top-Down Point Cloud with Conditional Neighborhood Aggregation for Multi-Gigapixel Histopathology Image Representation

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1. Acknowledgement

* Ali Bashashati and Hossein Farahani supervised the project. Ali Bashashati is the corresponding author.

2. Results

The complete results of survival prediction can be found in Tab. S1. These results confirm that our model has a consistent improvement compared to the baselines and across different architectures.

3. Baseline Implementation Details

For the implementation of the baselines, we used the official repository of Patch-GCN[1], which also included the implementation for the DeepSet, Attention MIL, and DGC methods. However, we added our own implementation of Variance MIL based on the Attention MIL. The hyperparameters were set to the suggested values in the paper [1], and we used the NLL loss [2] as suggested.

For the HIPT model, the pre-trained weights and model implementation were both taken from the official repository. A loss function similar to the one we used for our model (NLL loss) was used to train an MLP on top of the representation produced by the pre-trained model.

D-PCC (Density Preserving Deep Point Cloud Compression) was adapted from the official repository [2]. However, we added a middle layer at the bottleneck of the architecture to predict the hazards. Then, the model was trained using both the NLL and density preserving loss of the original model.

The DGCNN and PointNet were both included in the https://github.com/WangYueFt/dgcnn repository, which we used for our experiments.

For the HGSurvNet [4] we have done our implementation of the code as the source code for this paper was not published at the time of writing this manuscript.

[1] https://github.com/mahmoodlab/Patch-GCN
[2] https://github.com/yunhe20/D-PCC

4. Patient Risk Stratification Details

To stratify the patients, we took the median value of the predicted hazard for each patient across the 3 folds, resulting in a single predicted hazard for each patient. The hazard threshold was set to the nth quantile value of the collected hazards for all patients, where n is the ratio of the censored patients (patients who have survived). Finally, the patients are broken into low- and high-risk cohorts in comparison to this threshold.

5. Patient Stratification Curves

The survival curves for the TCGA-OV dataset can be found in S2. For the survival curves of the other datasets, please refer to the main text.

6. Cellular Graph Heatmap Visualization

We generated cellular graph heatmaps of our model for a set of low- and high-risk patients and visualized them in Figs. S3 and S4, respectively. Importantly, our model focuses more intently on areas of tumor epithelium with high tumour-infiltrating lymphocyte density in low-risk cases. This observation aligns with previous immunohistochemical, genomic, and transcriptomic studies that have shown better clinical outcomes in tumour-infiltrating lymphocyte-rich high-grade serous ovarian cancers [3, 4]. Conversely, in high-risk cases, our model displays a propensity to allocate attention toward dispersed tumor cells in areas without tumour-infiltrating lymphocytes.

References

[1] Richard J Chen, Ming Y Lu, Muhammad Shaban, Chengkuan Chen, Tiffany Y Chen, Drew FK Williamson, and Faisal Mahmood. Whole slide images are 2d point clouds: Context-aware survival prediction using patch-based graph convolutional networks. In *Medical Image Computing and Computer Assisted Intervention–MICCAI 2021: 24th International Conference, Strasbourg, France, September 27–October 1, 2021, Proceedings, Part VIII 24*, pages 339–349. Springer, 2021. 1

Type	Method	Feature Extractor	Parameters	HGSOC 1				HGSOC 2			
				C-Index (↑)	RMST (↑)	SRD@10 (↑)	P-value (↓)	C-Index (↑)	RMST (↑)	SRD@10 (↑)	P-value (↓)
Patch-Based	DeepSet	ResNet34	$395K$	0.475 ± 0.020	1.06	-4.6%	0.52	0.505 ± 0.019	1.29	$+0.7\%$	0.04
		ResNet50	$395K$	0.512 ± 0.038	0.66	-8.9%	0.53	0.446 ± 0.204	0.58	$+0.7\%$	0.86
	Attention MIL	ResNet34	$657K$	0.541 ± 0.040	1.88	$+11.9\%$	0.05	0.535 ± 0.025	1.52	$+3.4\%$	< 0.01
		ResNet50	$657K$	0.546 ± 0.017	1.41	-5.0%	0.12	0.510 ± 0.131	0.61	$+6.1\%$	0.12
	Variance MIL	ResNet34	$789K$	0.539 ± 0.051	0.86	$+3.5\%$	0.51	0.518 ± 0.017	1.49	$+6.9\%$	< 0.01
		ResNet50	$789K$	0.549 ± 0.015	1.39	-5.9%	0.37	0.505 ± 0.143	0.59	$+3.4\%$	0.37
	DGC	ResNet34	$658K$	0.502 ± 0.074	1.55	$+3.7\%$	0.41	0.524 ± 0.017	1.27	$+0.7\%$	0.05
		ResNet50	$789K$	0.549 ± 0.015	1.43	-3.7%	0.81	0.466 ± 0.177	0.56	-0.2%	0.59
	Patch-GCN	ResNet34	$1.3M$	0.522 ± 0.086	0.75	-4.4%	0.93	0.531 ± 0.017	1.49	$+6.1\%$	< 0.01
		ResNet50	$1.3M$	0.492 ± 0.058	0.60	-11.9%	0.24	0.482 ± 0.167	0.56	$+3.4\%$	0.39
	HIPT	Hierarchical ViT	$24M$	0.477 ± 0.034	0.66	$+1.6\%$	0.51	0.486 ± 0.007	0.95	$+3.3\%$	0.45
Point Cloud-Based	PointNet	ResNet34	$710K$	0.513 ± 0.033	1.18	$+12.2\%$	0.16	0.500 ± 0.012	0.77	-8.2%	< 0.01
	DGCNN	ResNet34	$1.9M$	0.519 ± 0.027	0.73	-3.9%	0.64	0.506 ± 0.022	1.11	$+5.3\%$	0.15
	DPCC	ResNet34	$17M$	0.505 ± 0.040	0.67	-6.5%	0.36	0.514 ± 0.025	1.14	$+5.7\%$	0.21
	CO-PILOT (Ours)	ResNet34	$356K$	$\mathbf{0.568 \pm 0.027}$	**2.29**	$\mathbf{+12.6\%}$	$\mathbf{< 0.01}$	$\mathbf{0.558 \pm 0.033}$	**1.61**	$\mathbf{+10.2\%}$	$\mathbf{< 0.01}$

Table S1: Survival prediction performance comparison of our model with all the baselines on two datasets.

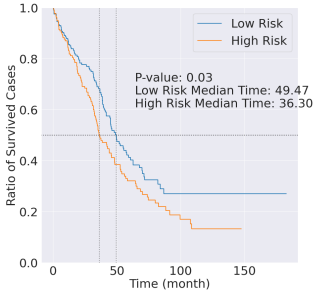
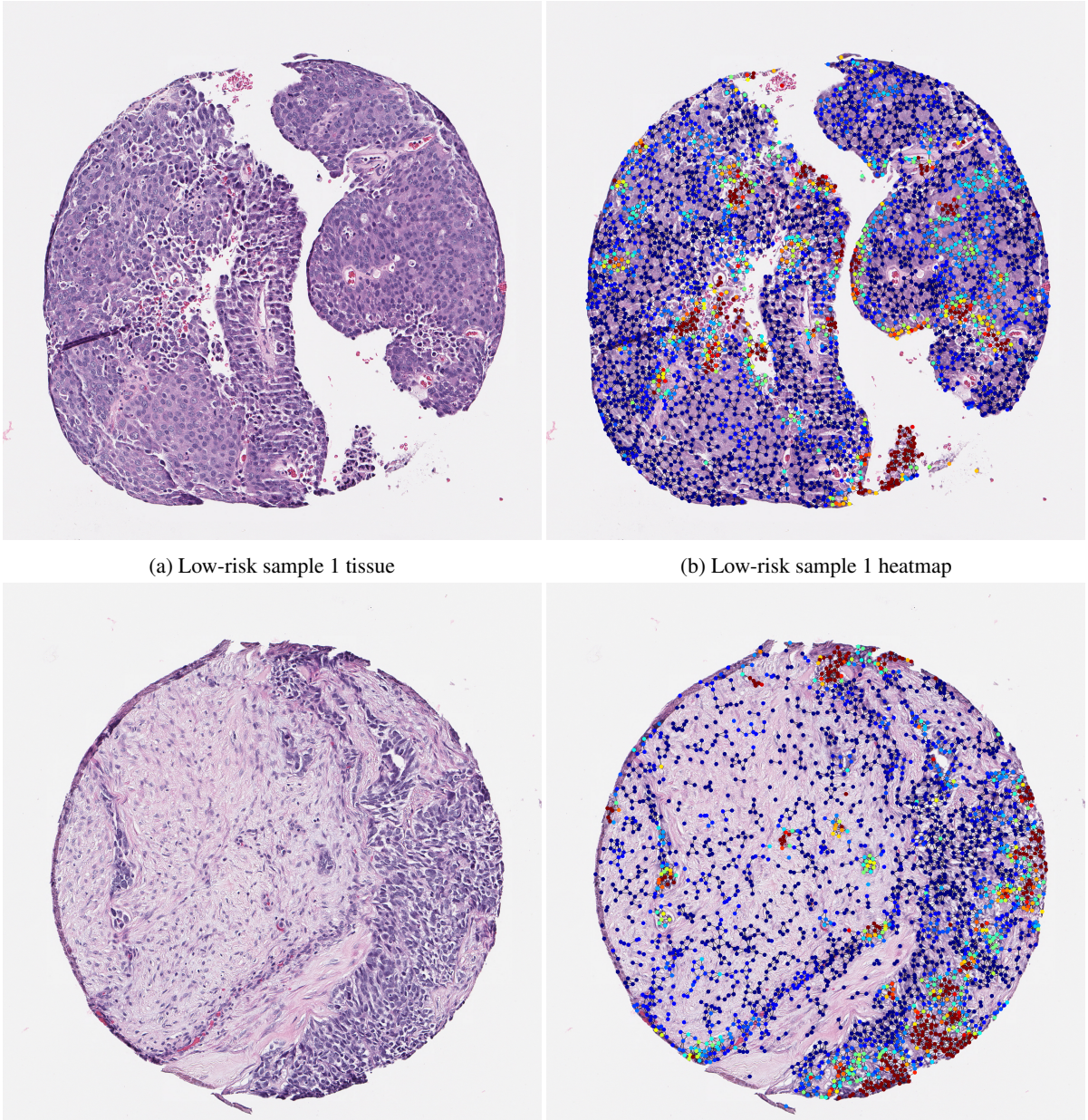


Figure S2: TCGA-OV patient stratification survival curve

[2] Shekoufeh Gorgi Zadeh and Matthias Schmid. Bias in cross-entropy-based training of deep survival networks. *IEEE transactions on pattern analysis and machine intelligence*, 43(9):3126–3137, 2020. 1

[3] Allen W Zhang, Andrew McPherson, Katy Milne, David R Kroeger, Phineas T Hamilton, Alex Miranda, Tyler Funnell, Nicole Little, Camila PE de Souza, Sonya Laan, et al. Interfaces of malignant and immunologic clonal dynamics in ovarian cancer. *Cell*, 173(7):1755–1769, 2018. 1

[4] Lin Zhang, Jose R Conejo-Garcia, Dionyssios Katsaros, Phyllis A Gimotty, Marco Massobrio, Giorgia Regnani, Antonis Makrigiannakis, Heidi Gray, Katia Schlienger, Michael N Liebman, et al. Intratumoral t cells, recurrence, and survival in epithelial ovarian cancer. *New England journal of medicine*, 348(3):203–213, 2003. 1



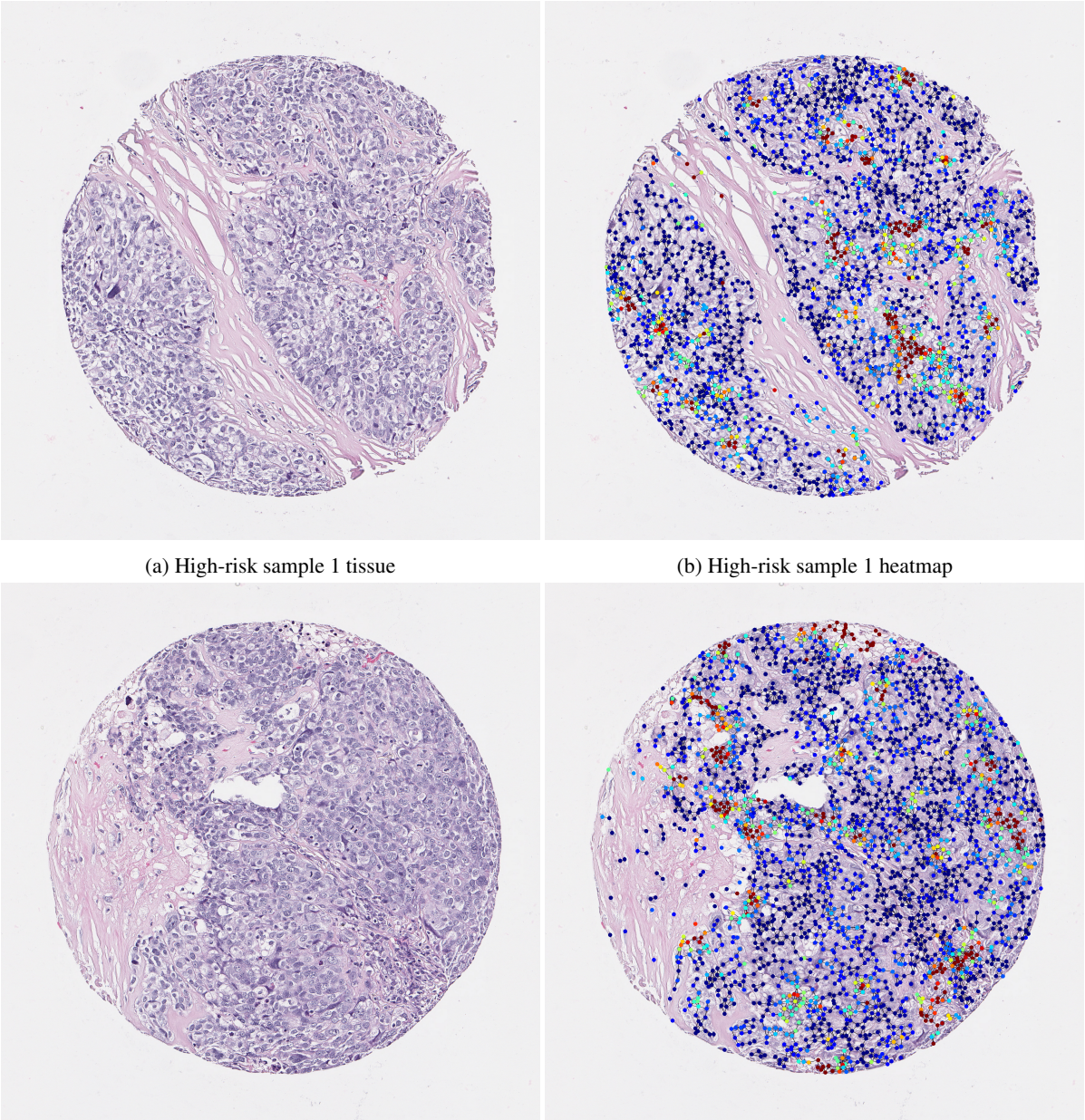
(a) Low-risk sample 1 tissue

(b) Low-risk sample 1 heatmap

(c) Low-risk sample 2 tissue

(d) Low-risk sample 2 heatmap

Figure S3: Cellular graph heatmap visualization of two low-risk cases



(a) High-risk sample 1 tissue

(b) High-risk sample 1 heatmap

(c) High-risk sample 2 tissue

(d) High-risk sample 2 heatmap

Figure S4: Cellular graph heatmap visualization of two high-risk cases