Deep Learning–Based Automated Tumor Cellularity Quantification in Triple-Negative Breast Cancer

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ABSTRACT

•Triple-negative breast cancer (TNBC) is an aggressive breast cancer subtype; accurate quantification of residual tumor is important for treatment-response assessment.

•Tumor cellularity is a key histopathologic measure but is manually estimated, making assessment time-intensive and susceptible to inter-observer variability

•Deep learning methods can automate tumor and cellular analysis from whole-slide images (WSIs), reducing reliance on manual annotation.

•We developed a computational pipeline integrating DeepLabV3-based tumor segmentation with alpha-shape tumor-bed delineation and HoVer-Net and CellViT nuclear detection/classification to quantify neoplastic cellularity within tumor regions.

INTRODUCTION

- **Triple-negative breast cancer (TNBC)** is an aggressive breast cancer subtype with limited targeted treatment options and a high risk of recurrence.
- **Neoadjuvant chemotherapy is commonly used** in TNBC, making accurate assessment of residual disease important for evaluating treatment response and prognosis.
- **Tumor cellularity quantifies the proportion of viable tumor cells within the tumor bed** and is an important component of histopathologic response assessment.
- **Current assessment relies on manual evaluation of H&E-stained tissue**, requiring pathologists to identify tumor regions and estimate cellularity; this process can be time-intensive and subject to inter-observer variability.
- **Whole-slide images (WSIs) contain extensive spatial and cellular information** that can be analyzed using deep learning to automate histopathologic assessment.
- **Combining tumor segmentation with nuclear detection and classification** enables automated identification of tumor regions and quantification of their cellular composition.
- **This study investigates a deep learning–based approach for reproducible tumor-bed delineation and cellularity quantification in TNBC WSIs.**

METHODS

Goal:
- Develop an automated deep learning pipeline to delineate tumor regions and quantify neoplastic cellularity in TNBC whole-slide images (WSIs).

Tumor Segmentation:
- Used a DeepLabV3-based segmentation model to classify WSI pixels into tissue classes.
- Downsampled segmentation maps 8× and isolated the tumor class to generate binary tumor masks.
- Applied morphological opening with an 8-pixel disk to remove small isolated regions and reduce segmentation noise.

Tumor Bed Delineation:
- Converted tumor pixels into a 2D spatial point cloud and constructed a radius-neighbor graph using a 30-pixel radius.
- Identified connected tumor components and removed components containing fewer than 1,000 points.
- Applied alpha-shape analysis with slide-specific parameters to generate boundaries around individual tumor foci and define the tumor bed.

Nuclear Detection & Classification:
- Used HoVer-Net and CellViT for nuclear segmentation and classification.
- Nuclear predictions provided cell coordinates, contours, predicted cell classes, and confidence scores.
- Classified nuclei into neoplastic, inflammatory, connective, necrotic, and benign epithelial populations.

Cellularity Analysis:
- Mapped nuclear centroids to the tumor-bed boundaries using point-in-polygon analysis.
- Calculated tumor cellularity as the proportion of neoplastic nuclei relative to all nuclei within the tumor bed.
- Additionally quantified the proportion of tumor-bed area occupied by neoplastic nuclear regions.

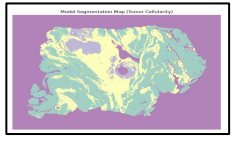


Figure 1: Tumor Mask done by DeepLabV3 Model

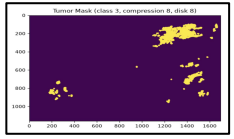


Figure 2: Binary tumor mask (class 3, compression 8, disk 8).

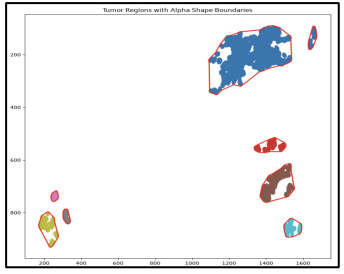
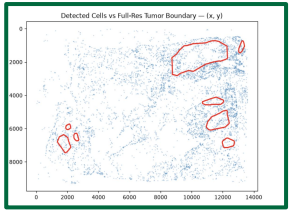
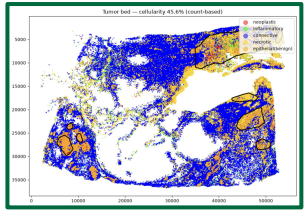


Figure 3: Alpha-shape boundaries fitted to each tumor cluster.

RESULTS





Cedars-Sinai Triple Negative Breast Cancer WSIs

File Name	CellViT Cellularity	HoVer-Net Cellularity (%)
2XKZb2Xuuacm.svs	11.11% (1 neoplastic / 9 total cells)	4.9% (19 neoplastic / 391 total cells)
6cSWNOb1bUcD.svs	43.97% (459 neoplastic / 1044 total cells)	20.5% (655 neoplastic / 3198 total cells)
B17nRVc7b7X.svs	3.57% (2 neoplastic / 56 total cells)	33.1% (5,175 neoplastic / 15,623 total cells)
DrjfQHLSDbMs.svs	37.31% (1843 neoplastic / 4940 total cells)	78.9% (285,069 neoplastic / 362,322 total cells)

National Cancer Institute Archive TNBC WSIs

File Name	Ground Truth Cellularity (%)	CellViT Cellularity (%)	HoVer-Net Cellularity (%)
102174.svs	20	18.36% (121 neoplastic / 659 total cells)	45.6% (65,462 neoplastic / 143,707 total cells)
99841.svs	35	15.83% (69 neoplastic / 436 total cells)	33.1% (18,228 neoplastic / 55,052 total cells)
99803.svs	70	74.23% (527 neoplastic / 710 total cells)	20.6% (7,431 neoplastic / 36,004 total cells)
99813.svs	90	8.82% (24 neoplastic / 272 total cells)	80.4% (120,057 neoplastic / 149,339 total cells)

CONCLUSION

Neither CellViT or HoVer_Net was reliably accurate. Both of them were significantly off for a couple of the archive images.

HoVer_Net consistently detects significantly more nuclei than CellViT for each slide, between 50-200 times more. However, HoVer_Net consistently took 60-90 minutes per .svs file to process versus less than one minute with CellViT

Both CellViT and HoVer_Net displayed inconsistent neoplastic cell densities between supposed tumor areas. This may result from image quality variances, or because of heterogeneous tumor subtypes which are harder for the models to distinguish.

Tuning these models for a specific institution's dataset and implementing a refined deep-learning pipeline has the potential to shorten the time between surgery and additional treatment for a patient.