A Deep Learning Method for Tumor Region Identification and Tumor Proportion Score Estimation for PD-L1 Expression in Non- Small Cell Lung Carcinoma

Purushottam Bhardwaj[1], Geetank Raipuria[1], Nidhi Bhatt[2]
[1]AIRAMatrix Private Limited, Mumbai, India [2]North Bristol NHS Trust, Bristol, UK

Overview

- PD-L1 (Programmed Death Ligand 1) protein expression has emerged as an important predictive biomarker for identifying patients with advanced lung cancer most likely to respond to immunotherapy.
- We propose a computational technique using Deep Learning for detecting the cancer regions and calculating the Tumor Proportion Score (TPS) for PD-L1 expression, in immunohistochemically stained sections from Non-Small Cell Lung Carcinoma (NSCLC).

Methods

- Tumor Proportion Score is the ratio between the PD-L1 positive tumor cells to the total tumor cell count. Thus, our proposed approach uses a two stage setup that first segments the tumor region from the tissue, followed by tumour cell instance segmentation.
- Tumor Region segmentation is performed using DeepLabV3+ [1] architecture. This eliminates regions including benign epithelium, lymphocytes, and necrosis, from the calculation of the TPS.
- At the second stage, we deploy a modified HoverNet [2] nuclei instance segmentation model that uses dual encoder with input at two different resolutions for greater context. The model categorises nuclei into PD-L1 positive, PD-L1 negative tumour cells, and lymphocytes, with the former two used for final scoring.

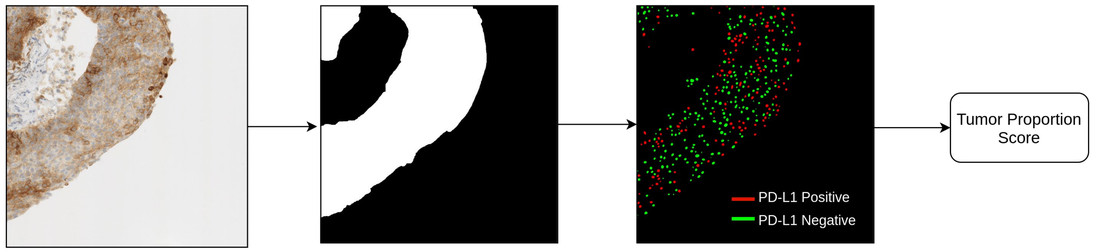

Figure 1: Proposed two stage Deep Learning model for counting PD-L1 positive and negative tumor cell nuclei

Dataset

- The Deep Learning models were trained using anonymised, de-identified Whole Slide Images (WSI) from 41 patients of NSCLC with varying PD-L1 scores. Anonymised, de-identified WSIs from another 57 patients were used as test data for pathological validation.
- WSIs with tumor region as well as nuclei boundaries, marked by expert pathologists, were used to train the Deep Learning models.

Results

- Our proposed approach achieved a sensitivity of 90.1% and specificity of 96.9% in cancer region segmentation.
- We evaluated the performance of the proposed dual stage approach at WSI level by comparing the TPS calculated by our computational method and that determined by an expert pathologist.
- We observed a Pearson's Coefficient of 0.91 that signifies a strong correlation between observations of the computational method and the pathologist.

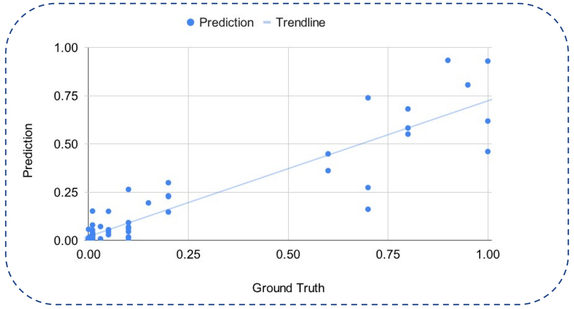

Figure 2: Predicted TPS score vs Pathologist score

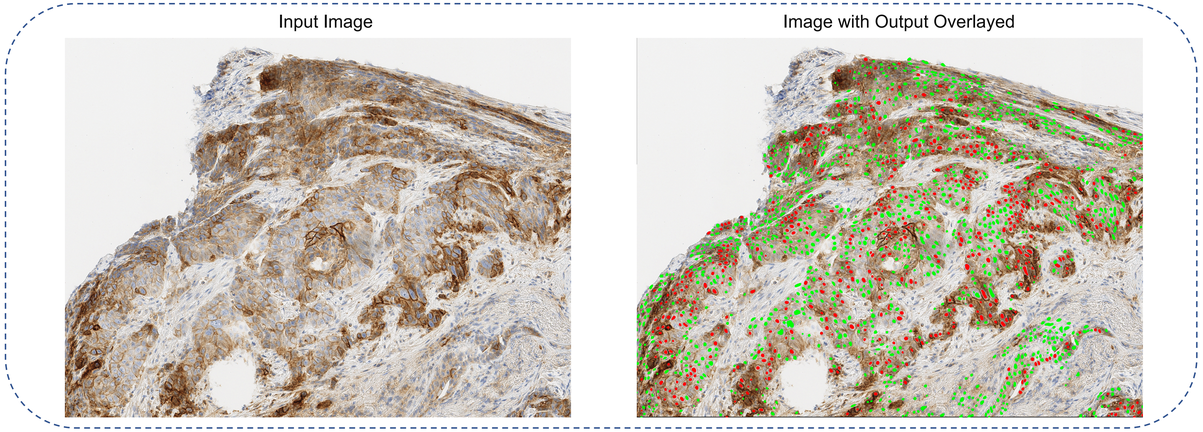

Figure 3: Sample prediction. Red and green color highlight predicted PD-L1 positive and negative tumor nuclei

Conclusion

We demonstrate the application of Deep Learning algorithms for rapid determination of PD-L1 expression on IHC stained Whole Slide Images of NSCLC, showing a high correlation with Tumor Proportion Score determined by expert pathologists (Pearson's Coefficient of 0.91).

References
[1] Chen, Liang-Chieh, et al. "Encoder-decoder with atrous separable convolution for semantic image segmentation." Proceedings of the European conference on computer vision (ECCV). 2018.
[2] Graham, Simon, et al. "Hover-net: Simultaneous segmentation and classification of nuclei in multi-tissue histology images." Medical Image Analysis 58 (2019): 101563.