SCENT: Multi Scale Ensemble Transformer for Non-Invasive Prediction of PD-L1 Expression and Response to Immune Checkpoint Inhibitors in NSCLC Using CT scans

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Abstract

Background: Immune checkpoint inhibitors (ICIs) are transformative in treating non-small cell lung cancer (NSCLC), benefitting 20–30% of patients. Nonetheless, the sole National Comprehensive Cancer Network (NCCN)-endorsed biomarker for ICI therapy initiation remains the Programmed Death-Ligand 1 (PD-L1) status determined by immunohistochemistry (IHC) on biopsy specimens. This study investigates a novel, non-invasive method for predicting PD-L1 expression in patients with metastatic NSCLC using chest computed tomography (CT) scans.

Purpose: We aimed to develop and validate the Scalable Ensemble Transformer (SCENT), a deep learning model that predicts PD-L1 expression from CT images, potentially obviating the need for invasive biopsy procedures.

Materials and Methods: This retrospective analysis encompassed two cohorts of stage IV metastatic NSCLC patients undergoing immunotherapy: 1080 individuals in total. Cohort 1 (n=746) served for discovery, training (n=298), tuning, internal validation (n=75), and testing (n=373). Cohort 2 (n=334), lacking prior PD-L1 measurements, was used for external validation. We employed SCENT to predict PD-L1 status and further stratify patients by progression-free survival (PFS) and overall survival (OS). The model's efficacy was compared against traditional 2D, 2.5D, and 3D models, as well as radiomics and clinical predictors.

Results: SCENT significantly outperformed existing models, achieving superior specificity (81.59%), sensitivity (82.14%), and area under the curve (AUC; 80.50%) in the testing set. Notably, the model maintained high performance across varying training set sizes, demonstrating its robustness and adaptability with an AUC of 82.1%. Importantly, SCENT's predictions of OS and PFS were comparable to those derived from IHC-based PD-L1 status, highlighting its potential as a viable alternative for invasive diagnostic methods.

Conclusion: The SCENT model represents a significant advancement in the non-invasive prediction of PD-L1 expression, with profound implications for the management of stage IV metastatic NSCLC. By potentially reducing the reliance on invasive biopsies, SCENT paves the way for more personalized and streamlined immunotherapy selection processes, marking a shift towards precision oncology.