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# Peritumoral CT Radiomics Encodes Tumor Biology Across Molecular, Immune and Clinical Endpoints in NSCLC

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**Introduction/Background**
Non-small cell lung cancer (NSCLC) management increasingly hinges on molecular and immune biomarkers. Yet these determinants still rely on invasive biopsies or sampling only a fraction of the tumor, often missing biology that drives progression. Radiomics converts routine CT imaging into quantitative phenotypes, but most studies remain anchored to the tumor core. Interest is growing to include the peritumoral tumor-stroma interface, precisely where oncogenic signaling, immune infiltration, and angiogenic remodeling concentrate. Here, we investigate whether imaging features derived from the peritumoral tumor-stroma interface serve as a radiographic surrogate for tumor biology and the immune microenvironment by capturing molecular (KRAS), immune (PD-L1) and clinical (recurrence, survival) phenotypes in a cohort of NSCLC patient images.

**Methods/Intervention**
Using the public TCIA NSCLC-Radiogenomics cohort (n=211 patient), we extracted PyRadiomics features under four matched regions: intra-tumor core, peritumoral ring, cumulative (core+ring), and concatenated (core⊕ring features). Four biologically distinct endpoints were interrogated where available: KRAS mutation, PD-L1/CD274 high-vs-low, recurrence, and survival. Significance screening, correlation pruning, consensus nested cross-validation selection, scaling, and oversampling steps ran strictly within folds against a mandatory chance-level reference; smoking status was tested as a secondary multimodal comparison. Discrimination used ROC-AUC across twelve classifiers.

**Results/Outcome**
The peritumoral region consistently matched or surpassed the tumor core across all endpoints. Peritumoral features were the single best CT biomarker assessed for KRAS and PD-L1/CD274 (AUCs 0.748 (95% CI, 0.65, 0.82), 0.808 (95% CI, 0.70, 0.84) respectively). Peritumoral features performed similarly or better than any other feature groups for both survival and recurrence. Discrimination was driven by higher-order texture (GLSZM, NGTDM, GLRLM) and wavelet/LoG features, consistent with stromal remodeling, necrosis, and interface complexity rather than gross tumor size. Adding clinical variables produced only modest, non-transformative gains.

**Conclusion**
Under leakage-aware validation, peritumoral CT texture carries molecular (KRAS), immune (PD-L1) and prognostic (recurrence, survival) signal comparable to or exceeding the tumor core across independent endpoints. These results indicate that imaging features may serve as a strong radiographic surrogate for tumor biology and the surrounding immune microenvironment.

## Statement of Impact

Sampling the peritumoral microenvironment, not just the tumor core, yields consistent non-invasive readouts of genotype, immune status, and outcome in NSCLC.


## Keywords

tumor biology; radiomics; tumor microenvironment; imaging biomarkers; NSCLC; translational research