An interpretable AI-derived radiology signature to identify patients at risk of progression on the PACIFIC regimen for unresectable non-small cell lung cancer

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Background:

Advances in the treatment of unresectable NSCLC have emerged through the combination of chemotherapy, radiotherapy, and immune checkpoint inhibitors (ICI), also known as the PACIFIC regimen. Despite this protocol's benefits, it lacks predictive biomarkers and many patients will ultimately fail to respond. Artificial intelligence (AI) has shown promise in identifying patients responsive to ICI, but its ability to identify patients who may not benefit from such combination regimens remains underexplored. We introduce an AI-enabled approach leveraging interpretable imaging biomarkers, such as tumor heterogeneity and twistedness of the tumor-associated vasculature, to identify patients who will fail to benefit from chemo-radio-immunotherapy (CRIT) using pretreatment scans.

Methods:

We analyzed CT data from 148 NSCLC patients with predominantly stage III (91%) disease from two institutions. Target lesions were delineated by a trained radiologist. The Picture Health Px platform was utilized to segment the lungs and pulmonary vessels. Subsequently, a number of interpretable imaging features from the tumor and surrounding tissues were extracted. A Cox proportional hazards model of feature clusters was developed on the training set (n=101) to stratify patients into benefit groups associated with progression-free survival (PFS). A cohort of 47 patients receiving CRIT were held out for testing.

Results:

The imaging-derived high-risk group defined by the model was associated with decreased PFS in the test set, with a hazard ratio (HR) of 4.99 (95% CI: 2.04-12.18; $p<0.005$) and concordance index (C-index) of 0.66. The risk groups identified by the model outperformed PD-L1 negative status in identifying likely progressors (C-index=0.52; HR=1.49 [0.51-4.54], $p=0.47$), and were additionally independently prognostic of PD-L1 status when compared in a multivariable analysis ($p<0.001$). The primary features driving the model were measurements of the radius and tortuosity of the tumor-associated vasculature, as well as heterogeneity metrics of the tumor.

Conclusion:

An AI imaging tool that stratifies patients by risk after CRIT from baseline radiology was developed. The tool was able to strongly identify a subset of patients at very high risk of progression if treated with CRIT. These risk groups outperformed PD-L1 and thus may address biomarker gaps in the CRIT setting. With further clinical validation, radiology-based risk stratification could be used to identify a subset of unresectable NSCLC patients for whom alternatives to the standard of care should be explored.