

AI-powered radiomics model predicts immune checkpoint inhibitor-related pneumonitis (CIP) in advanced NSCLC patients

Seyoung Lee², Amogh Hiremath⁹, Jeeyeon Lee², Peter Haseok Kim³, Kai Zhang⁹, Salie Lee, Monica Yadav¹, Maria Jose Aguilera Chuchuca¹, Taegyum Um¹, Myungwoo Nam⁴, Liam Il-Young Chung¹, Hye Sung Kim¹, Jisang Yu¹, Trie Arni Djunadi¹, Leeseul Kim⁴, Youjin Oh¹, Sungmi Yoon⁵, Zunairah Shah⁶, Yuchan Kim¹, Ilene Hong¹, Grace Kang¹, Jessica Jang¹, Amy Cho¹, Soowon Lee⁷, Cecilia Nam⁸, Timothy Hong⁸, Yury S. Velichko¹, Vamsidhar Velcheti¹⁰, Anant Madabhushi⁹, Nathaniel Braman⁹, Young Kwang Chae¹

¹ Feinberg School of Medicine, Northwestern University, Chicago, IL, USA; ² School of Medicine, Kyungpook National University, Daegu, Republic of Korea; ³ The University of Texas at Austin, Austin, TX, USA; ⁴ Lincoln Medical and Mental Health Center, Bronx, NY, USA; ⁴ Ascension Saint Francis Hospital Evanston, Evanston, IL, USA; ⁵ New York City Health and Hospitals Corporation North Central Bronx/Jacobi Medical Center, NY, USA; ⁶ Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA; ⁷ Baylor University, TX, USA; ⁸ Northwestern University, Evanston, IL, USA; ⁹ Picture Health, Cleveland, OH, USA; ¹⁰ Laura and Isaac Perlmutter Cancer Center, New York University Langone Health, New York, NY, USA

Background: With the escalating integration of immunotherapy in the management of advanced non-small cell lung cancer (NSCLC), the emergence of adverse events, particularly immune checkpoint inhibitor-related pneumonitis (CIP), poses important challenges. CIP is not uncommon and can be life-threatening. It often necessitates the discontinuation of immunotherapy, even in patients with an otherwise favorable response. Prevention, early detection and early management of CIP can enhance patient outcomes, yet no such predictive models have been established. This study investigates the use of Artificial Intelligence (AI) algorithms in analyzing radiomic features for the prediction of CIP in NSCLC patients receiving immunotherapy.

Methods: A cohort of 105 stage III-IV NSCLC patients receiving immunotherapy was examined. Half of the patients were randomly

split to a training set, while the remaining half were reserved for algorithm testing. The manual segmentation was performed by three physicians annotating in consensus using LIFEx software v7.3.0 (IMIV/CEA, Orsay, France). The Picture Health Px platform was utilized to perform an AI-powered deep phenotyping of the tumor and its surrounding habitat. A number of interpretable feature measures were extracted from baseline CT scans, which were in turn used to train a deep learning classifier for the detection of pneumonitis. Weighting techniques were applied to compensate for the imbalance of pneumonitis cases.

Results: Among the 105 patients, 63 (60.0%) received immunotherapy-only regimen and 42 (40.0%) received combination immunochemotherapy. 18 (17.1%) patients had pneumonitis events. Within this subset, 10 (55.6%) had CIP. Among the CIP group, six patients (60.0%) had grade 1 pneumonitis, three patients (30.0%) had grade 2 pneumonitis, and one patient (10.0%) had grade 3 pneumonitis, and none had grade 4 or grade 5 pneumonitis. Within the training set (n=51), the cross-validated area under the ROC curve (AUC) was 0.71 (95% CI: 0.68-0.74). When applied to the test set, the model predicted pneumonitis with AUC=0.63. Across the two datasets, the model correctly identified 4/6 (66.7%) grade 1 pneumonitis events and 2/3 (66.7%) grade 2 pneumonitis events, but misclassified the only available grade 3 event.

Conclusion: The utilization of CT-based radiomic features demonstrates promise in predicting CIP in NSCLC patients undergoing immunotherapy. This approach holds potential for enhancing the identification and management of CIP, among NSCLC patients treated with immunotherapy.