AI may help predict responses to non-small cell lung cancer systemic therapies

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Using standard-of-care computed tomography (CT) scans in patients with advanced non-small cell lung cancer (NSCLC), researchers utilized artificial intelligence (AI) to train algorithms to predict tumor sensitivity to three systemic cancer therapies.

The study is published in *Clinical Cancer Research*, a journal of the American Association for Cancer Research, by Laurent Dercle, MD, Ph.D., associate research scientist in the Department of Radiology at the Columbia University Irving Medical Center

"Radiologists' interpretation of CT scans of cancer patients treated with systemic therapies is inherently subjective," said Dercle. "The purpose of this study was to train cutting-edge AI technologies to predict patients' responses to treatment, allowing radiologists to deliver more accurate and reproducible predictions of treatment efficacy at an early stage of the disease."

To determine if patients with NSCLC are responding to systemic therapy, radiologists currently quantify changes in tumor size and the appearance of new tumor lesions, Dercle explained. However, this type of evaluation can be limited, especially in patients treated with immunotherapy, who can display atypical patterns of response and progression, he noted. "Newer systemic therapies prompt the need for alternative metrics for response assessment, which can shape therapeutic decision-making," Dercle said.

Dercle and colleagues utilized data from multiple phase II/phase III clinical trials that evaluated systemic treatment in patients with NSCLC. These patients were treated with one of three agents: the immunotherapeutic agent nivolumab (Opdivo), the chemotherapeutic agent docetaxel (Taxotere), or the targeted therapeutic gefitinib (Iressa). The researchers retrospectively analyzed standard-of-care CT images from 92 patients receiving nivolumab in two trials; 50 patients receiving docetaxel in one trial; and 46 patients receiving gefitinib in one trial.

To develop the model, the researchers used the CT images taken at baseline and on first-treatment assessment (three weeks for patients treated with gefitinib; eight weeks for patients treated with either nivolumab or docetaxel). Tumors were classified as treatment-sensitive or treatment-insensitive based on the reference standard of each trial (median progression-free survival in the nivolumab and docetaxel cohorts; analysis of surgical specimen following gefitinib treatment). Among all three cohorts, patients were randomized into training or

validation groups.

The researchers used machine learning to develop a multivariable model to predict treatment sensitivity in the training cohort. Each model could predict a score ranging from zero (highest treatment sensitivity) to one (highest treatment insensitivity) based on the change of the largest measurable lung lesion identified at baseline.

Because the gefitinib cohort had a limited number of patients, the researchers built and validated a model using a cohort of metastatic colorectal cancer patients (302 individuals) treated with anti-EGFR therapies. The radiologic features to predict treatment sensitivity identified in the colorectal cancer cohort were then used to build a model in the training cohort of patients with NSCLC treated with gefitinib.

Across all cohorts, a total of eight radiologic features were used to build the three prediction models. These features included changes in tumor volume, heterogeneity, shape, and margin. Both the nivolumab and gefitinib models used four radiologic features, and the docetaxel model used one.

The performance of each signature was evaluated by calculating the area under the curve (AUC), a measure of the model's accuracy, where a score of 1 corresponds to perfect prediction. The nivolumab, docetaxel, and gefitinib prediction models achieved an AUC of 0.77, 0.67, and 0.82 in the validation cohorts, respectively.

"We observed that similar radiomics features predicted three different drug responses in patients with NSCLC," Dercle said. "Further, we found that the same four features that identified EGFR treatment sensitivity for patients with metastatic colorectal cancer could be utilized to predict treatment sensitivity for patients with metastatic NSCLC."

Dercle noted that radiomic signatures offer the potential to enhance clinical decision-making. "With AI, cancer imaging can move from an inherently subjective tool to a quantitative and objective asset for precision medicine approaches," he said.

Limitations of the study include the small sample size. "Because AI can continuously learn from real-world data, using AI on larger patient datasets will help us to identify new patterns to build more accurate prediction models," noted Dercle.

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