

A Non-invasive Computational Imaging Approach May Help Predict Response to Immunotherapy

PHILADELPHIA — A computational imaging-based signature of immune-cell infiltration in and around a tumor could predict patients' responses to treatment with anti-PD1/PDL1 immunotherapies, according to data from a study presented at the [AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics](#), held Oct. 26-30.

“Immunotherapy, a recent modality of treatment in oncology, has profoundly changed the management of multiple cancers,” said Roger Sun, MD, PhD candidate under Eric Deutsch (MD, PhD) and Charles Ferté (MD, PhD), at the laboratory INSERM U1030 at Gustave Roussy in Villejuif, France. “However, most patients do not respond to this type of treatment. That is why we need to identify biomarkers that allow identification of patients who are most likely to respond to immunotherapy.”

Studies using biopsy samples of tumor tissues have shown that the extent of immune-cell infiltration into tumors correlates with patients' treatment responses. But because cancers are heterogeneous, biopsies only reflect the local aspect of the tumor, Sun explained. “Medical computational imaging, also known as radiomics, is a new field of research that aims to translate standard imaging like CT, MRI, or PET, into objective data, and use them as biomarkers,” he said. “This kind of biomarker is noninvasive, cost-effective, can be applied on all tumor localizations, and can be repeated through the course of disease.”

Sun and colleagues used radiomics to estimate the abundance of immune-cell infiltration in tumors and assess their potential to predict response to anti-PD1/PDL1 therapies. The team developed a radiomics-based model of tumor-infiltrating effector T cells (Teff) using data from the head and neck, liver, lung, and bladder cohorts of [The Cancer Imaging Archive](#). They extracted 80 radiomics features and built a radiomics score that could predict the abundance of tumor-infiltrating Teff estimated using RNAseq data.

To validate the radiomics score they developed, they first tested it on the CT scans of a cohort of 134 patients for whom RNAseq data were available. They found that the radiomics score of Teff correlated with the genomics-based score of Teff.

They then tested the radiomics score on the baseline CT scans of a second cohort of 137 patients enrolled in anti-PD1/PDL1 phase I trials for whom survival data were available.

The researchers applied the radiomics score on data from the entire cohort and used the median value to separate the cohort into two groups: those whose scores were above the median and those whose scores were below the median. They found that at any given time point, patients with a high score were 1.5 times more likely to be alive compared with those who had a low score.

“We are very encouraged by our findings that a signature based on imaging features could reflect the tumor immune infiltration and could predict response to immunotherapy,” Sun said. “These results are preliminary, and we need further clinical studies to validate them. Ultimately, this score may be useful to drive immunotherapy trials allowing stratification of patients.”

Sun added, “Enhancing data sharing and facilitating patient recruitment in clinical trials are necessary. With further improvements to this field with multi-disciplinary working groups, radiomics can become a reliable part of the decision support system in oncology.”

A limitation of the study is that the scores were validated using cohorts of limited size and medical images from different centers with heterogeneous acquisition protocols. “We still need to validate it using large cohorts of patients and standardized imaging protocols,” Sun noted.

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Presentation Session: [SPR02 – Spotlight on Proffered Papers Session 2: Immunogenomics and Response to Immunotherapy](#); Friday, Oct. 27; 6:30-7:15 p.m. ET; Terrace Ballroom, 400 Level

Title: Prediction of clinical outcomes of cancer patients treated with anti-PD-1/PD-L1 using a radiomics-based imaging score of immune infiltrate

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Background: The discovery of biomarkers identifying responders to immunotherapy is a major challenge. Tumor and peritumoral immune infiltration has been shown to be associated with response to anti-PD-1/PD-L1. The aim of this study was to develop a radiomics-based imaging tool of tumor immune infiltrate and to assess whether such a tool could predict clinical outcomes of patients treated with anti-PD1/PDL1.

Methods: A predictive radiomics-based model of tumor-infiltrating CD8+ T cells was trained using data from the head and neck cohort of The Cancer Imaging Archive (HNSC-TCIA). Two cohorts from our institute were used for validation. Contrast-enhanced CTs of 57 patients from the HNSC-TCIA were manually segmented (tumor and surrounding tissue) and 76 radiomics features extracted. A radiomics-based score was build using radiomics features to predict tumor-infiltrating CD8+ T-cells' abundance, which was estimated using RNA-sequencing data from The Cancer Genome Atlas, and the Microenvironment Cell Populations-counter signature. As a first validation, this signature was applied to an independent cohort of 100 patients for whom the pathologic tumor immune infiltrate was postulated as

either favorable (lymphoma, melanoma, lung, bladder, renal, MSI+ cancers, and adenopathy; 70 patients) or unfavorable (adenoid cystic carcinoma, low-grade neuroendocrine tumors, uterine leiomyoma; 30 patients). The signature was then applied on baseline-CTs of a second external cohort of 139 patients prospectively enrolled in anti PD-1/PD-L1 phase 1 trials. The median of the radiomics-based CD8+ score was used to separate patients into two groups (high and low score). Survival was estimated using Cox-proportional hazards model.

Results: We developed a radiomics-based CD8+ signature using the six radiomics features that had highest performance on random forest. In the first external cohort, the radiomics-based CD8 T-cells score was associated with the postulated tumor immune infiltrate (Wilcoxon test, $P < 0.001$). In the second external cohort of patients treated with anti-PD-1/anti-PD-L1, median (\pm SD) radiomics score was 109.6 ± 61.3 . Patients with high-predicted score had significantly better OS (HR= 0.55, 95%CI=0.36-0.86, $P= 0.009$). The radiomics-based CD8+ predicted score remained significant in a multivariate Cox regression analysis including RMH score (HR= 0.50, 95%CI=0.32-0.78, $P= 0.003$).

Conclusions: The radiomics-based signature of CD8+ T cells appears as a promising tool to estimate tumor immune infiltrate and to infer the outcome of patients treated with anti-PD-1/PD-L1.

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