Machine learning-based signature integrating radiomics and clinical data predicts response to immune checkpoint inhibitors in solid tumors.


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Background
There is a need for predictive biomarkers of response to immune checkpoint inhibitors. This study aims to develop and validate a signature combining advanced computational image analysis and clinical data to predict the response to immune checkpoint inhibitors in patients with advanced solid tumors including prostate cancer.

Methods
In this retrospective study, a predictive signature was derived from 239 metastatic lesions from 85 consecutive patients treated with immune checkpoint inhibitors (programmed-death protein 1 [PD-1] or programmed-death ligand 1 [PD-L1] inhibitors) monotherapy in phase I clinical trials from August 2012 to May 2018 (Cohort 1). External validation was performed in 112 lesions from 46 consecutive patients with urinary bladder cancer treated with anti-PD-1 or PD-L1 monotherapy (Cohort 2). All lesions per patient in the pre-treatment CT scan were semi-automatically delineated. Radiomics variables of first-order, shape, and texture were extracted and an elastic-net model was implemented to predict response. A linear model was used to combine radiomics and clinical variables. Further biological validation was pursued studying the association (Mann-Whitney analyses) of radiomics score with tumor-lymphocyte infiltration and RNA signatures of cytotoxic cells.

Results
In the Cohort 1 (training set), the radiomics signature associated with response (AUC of 0.74; \( P<0.001 \)). In the Cohort 2 (validation set), the radiomics signature predicted a response with an AUC of 0.70 (\( P=0.001 \)). Tumor homogeneity and spherical shape, corresponding to a high radiomics-signature score, are predictive of tumor response. The model combining radiomics and clinical features had an AUC of 0.76 (\( P<0.001 \)) in the training set and an AUC of 0.78 (\( P<0.001 \)) in the validation set. High radiomic score associated with cytotoxic-enriched immunophenotype (\( P=0.035 \)).

Conclusions
CT-radiomics signature at baseline predicts the response to immune checkpoint inhibitors and reflects the tumor immunophenotype in solid tumors including prostate cancer. Integrating radiomics and clinical data improve the prediction performance.

Conflict of Interest
The authors have no conflict of interest to declare in relation to this work.
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