

Predicting CD8 + T Cell Infiltration and PD-L1 Expression in renal cell RCC CT Radiomic Signatures

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Conflict of Interest Disclosure

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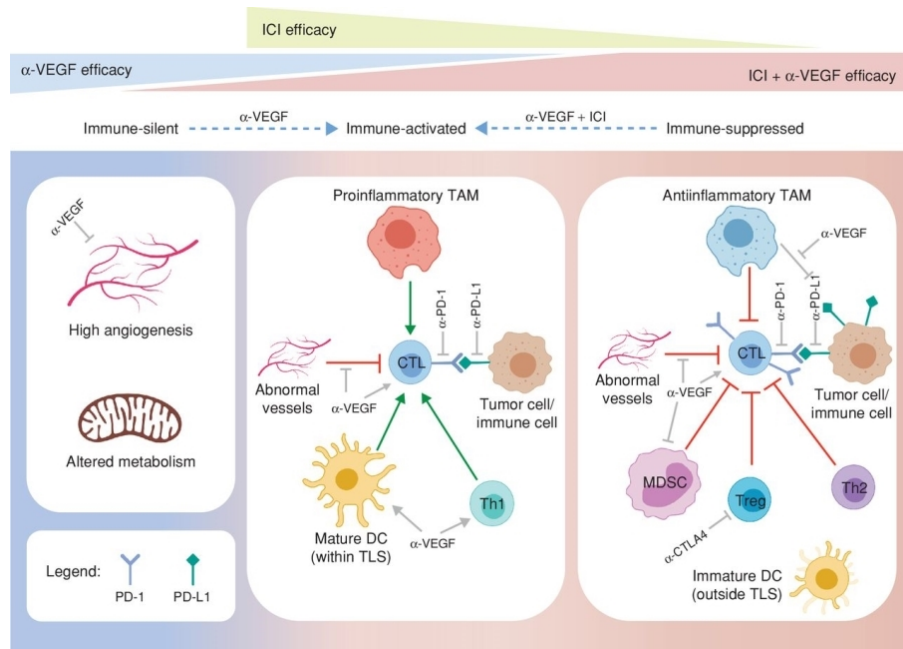
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Introduction

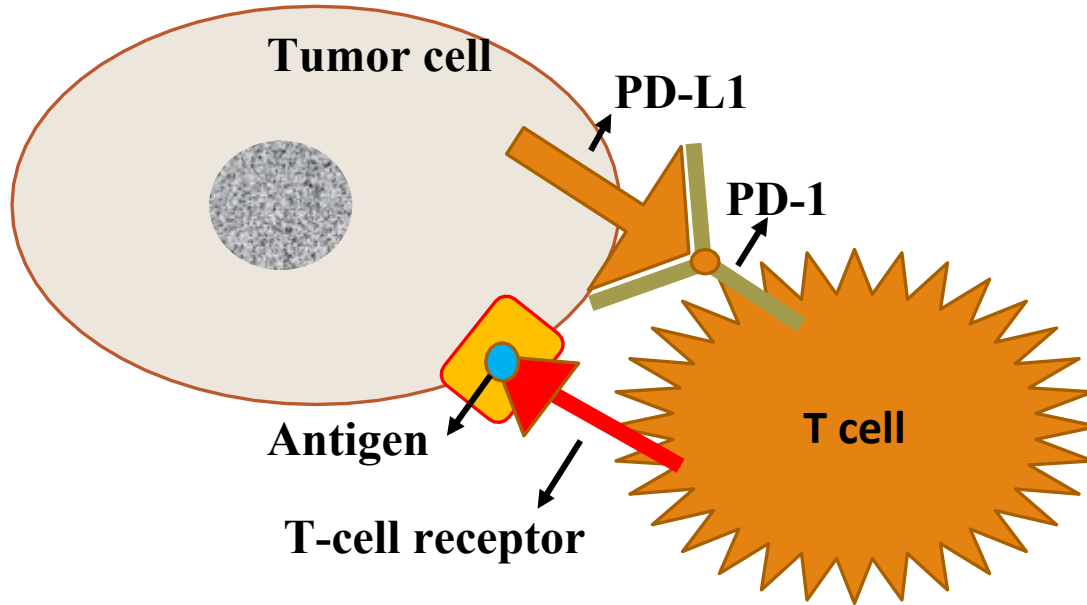
Immune checkpoint inhibitor (ICI) based therapies have become a standard of care for treatment naïve RCC patients

Biomarkers are needed for appropriate patient selection

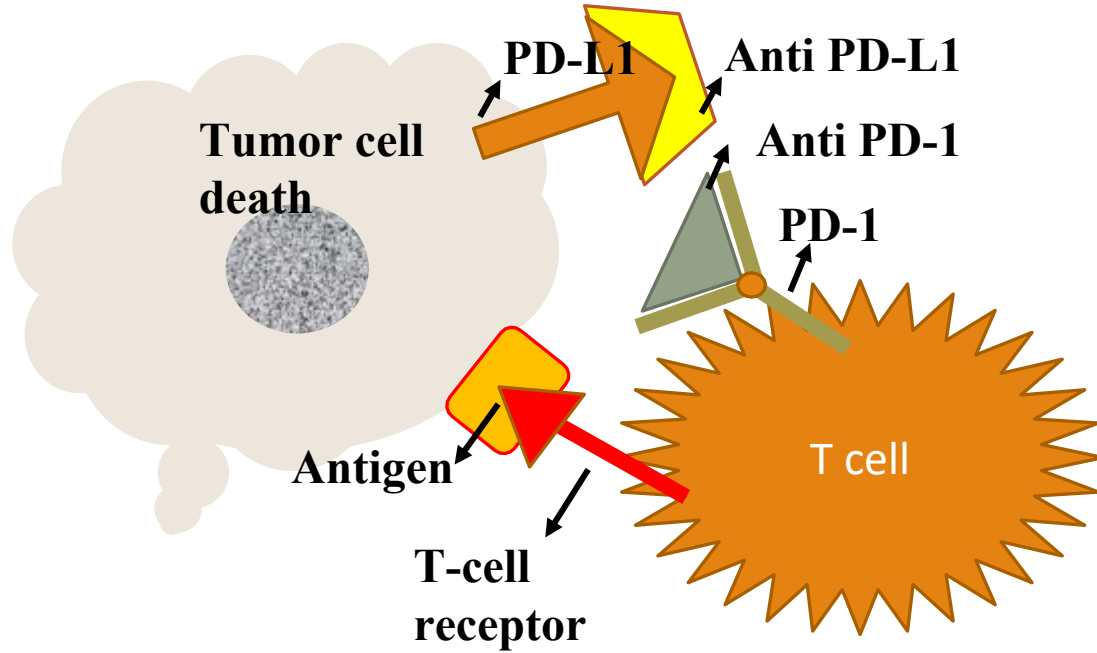
CD8 T cell infiltration and PD-L1 expression in the tumor are potential markers of response to ICI



Introduction



Introduction



Methods

Patient Cohort

Retrospective study (June 2009-2018)

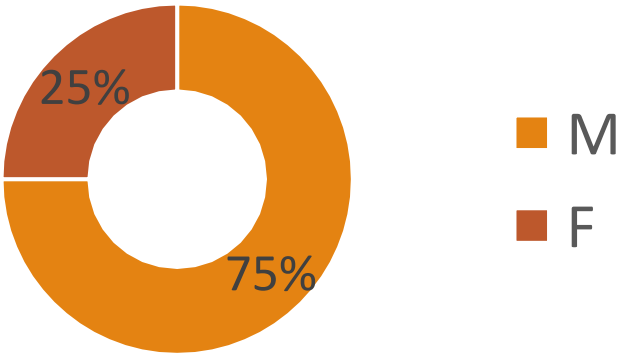
- IRB approved
- HIPAA compliant

Patients with pathologically confirmed ccRCC with:

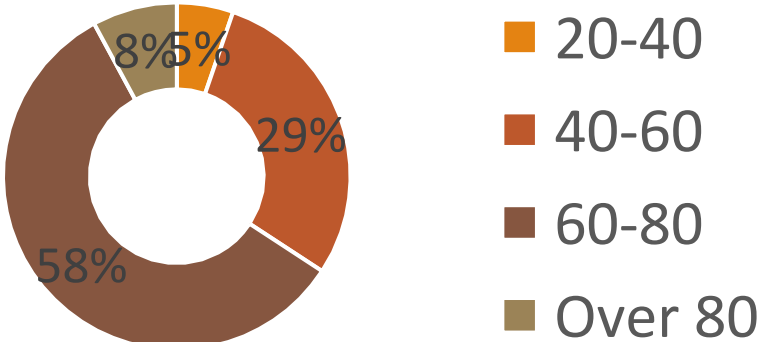
- preoperative multiphase CT
- available tumor resection specimens

ccRCC Cohort Demographics

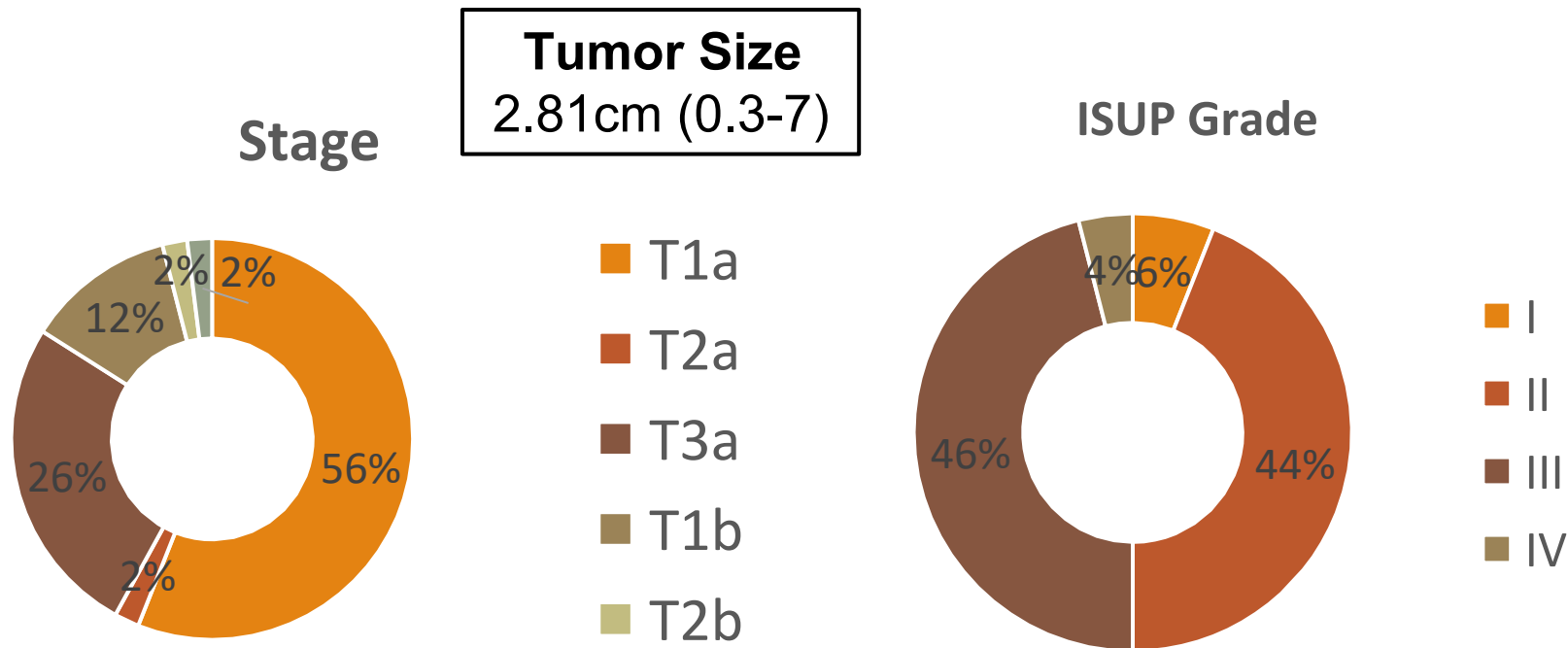
Gender



Age



ccRCC Cohort Distribution



Methods

Immuno-histochemistry

- CD8+ T cells
- PD-L1



Radiomics

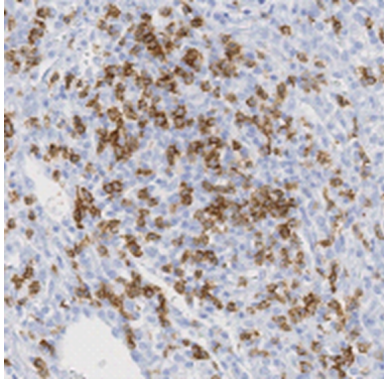
- Tumor volume manually segmented from CT
- Custom Matlab-based radiomics panel (1708 metrics) to create radiomic signatures.



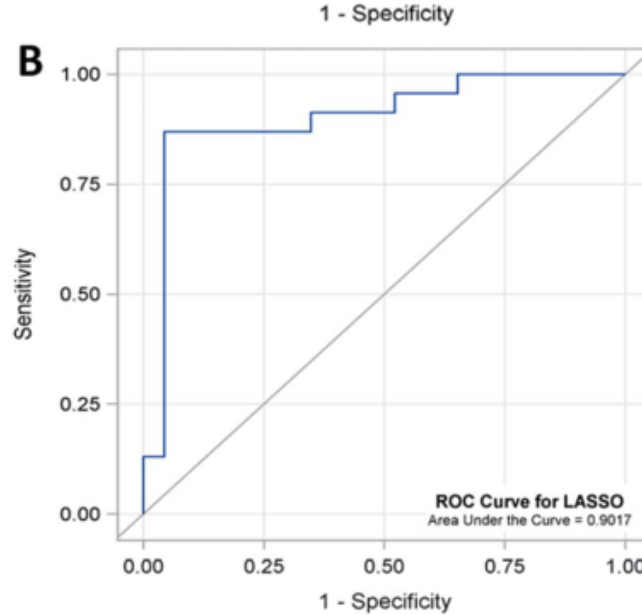
ROC analysis (AUC)

- Based on predicted probability from multiple iterations of leave-one-out cross-validation testing data

Results: CD8 Infiltration



**IHC with antiCD8
monoclonal antibody
clone 4B11**



**ROC for predicting
CD8 infiltration with
a cutoff of 80 cells/hpf**

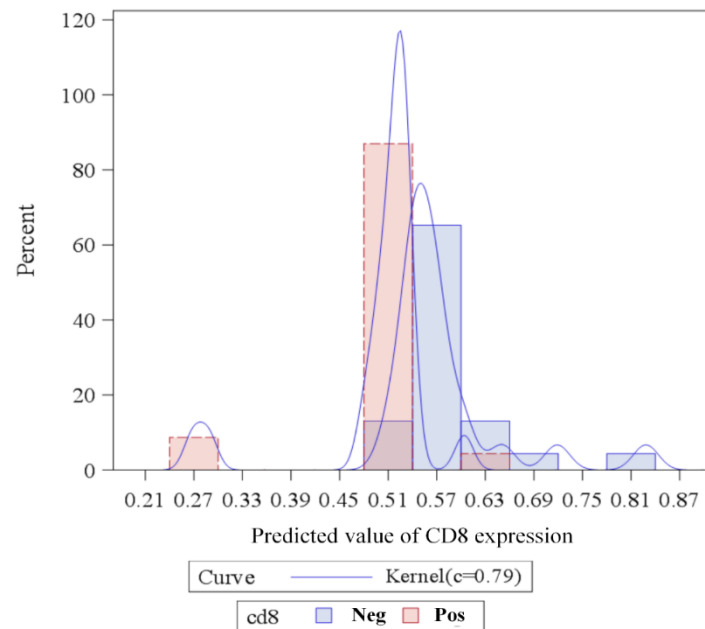
Immunohistochemistry (IHC) for CD8+ T cells (Leica Bond-III automated IHC platform using Bio-Rad anti-CD8 monoclonal antibody clone 4B11) and PD-L1 (Leica Bond-III automated IHC platform using Abcam anti-PD-L1 monoclonal antibody clone 28-8) was performed

Predicting CD8+ T Cell infiltration in ccRCC

48 patients with ccRCC
25 CD8 + and 23 CD8 - based on IHC counts of 80

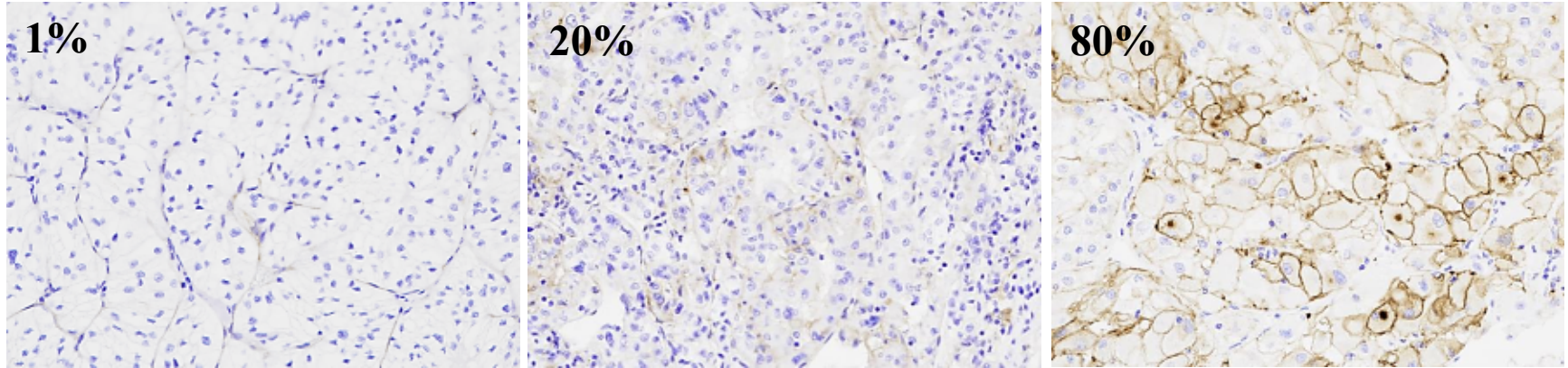
48 iterations of LOOCV testing data showed an AUC of 0.9; 95% CI; 0.8-1 in discriminating patients with CD8-positive from CD8-negative infiltration.

Distribution of predicted probability using histogram showed almost complete separation between CD8-positive and CD8-negative around 0.5.



Predicted probability of CD8 infiltration by CD8 positive vs. CD8 negative cases

PD-L1 Expression in RCC



Immunohistochemical quantitation of PD-L1 expression in RCC.

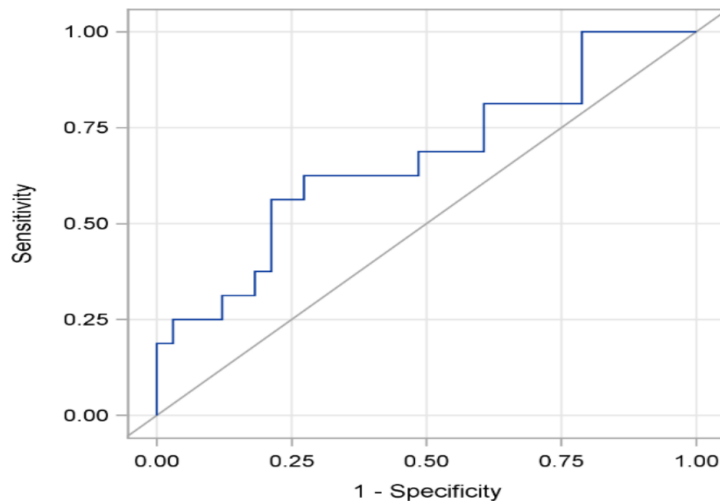
Technique: Tissue sections were stained with PD-L1 (clone 28-8, Abcam) on a Leica Bond autostainer. The percentage of tumor cells showing partial or complete membrane staining at any intensity (tumor proportion score) was determined.

Representative IHE cases with 1%, 20%, and 80% staining are shown.

PDL1 expression and Radiomics in ccRCC

50 patients with ccRCC: 16 were PDL1+, 34 PDL1 –

The result from 50 iterations of leave-one-out testing data showed an **AUC of 0.67**; 95% CI; 0.5-0.84 for AdaBoost classifier to discriminate between positive and negative PD-L1 expression groups. Of the various radiomic metrics, variance, kurtosis and skewness extracted from the 2nd and 4th band of Haar wavelet transformed pre-contrast, nephrographic and excretory phase were of high ranking importance.



CT-based radiomic metrics can differentiate positive- from negative- PD-L1 expression in ccRCC patients with an AUC of 0.67

Conclusions

- CT-based radiomic signatures can predict CD8+ T cells and PD-L1 expression in ccRCC
- This is being validated currently in an internal, as well as external, validation cohort

Conclusions

- This analysis can potentially negate the biases of sampling biases during a biopsy
- The implications for management are significant in that the radiomic signatures could differentiate tumors and patients more likely to respond to checkpoint inhibitor therapy

Thank You

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