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

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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.

Tumeh et al. Nature 2015; Motzer et al. NEJM 2018; Vuong et al Cancer Disco 2019
Introduction

Tumor cell

PD-L1

PD-1

Antigen

T-cell receptor

T cell
Introduction

T cell

Tumor cell death

Antigen

T-cell receptor

PD-L1

Anti PD-L1

Anti PD-1

PD-1

T cell
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
- M: 75%
- F: 25%

Age
- 20-40: 58%
- 40-60: 29%
- 60-80: 8%
- Over 80: 5%
ccRCC Cohort Distribution

**Tumor Size**  
2.81cm (0.3-7)

**Stage**  
- T1a: 56%  
- T2a: 12%  
- T3a: 6%  
- T1b: 2%  
- T2b: 2%

**ISUP Grade**  
- I: 46%  
- II: 44%  
- III: 4%  
- IV: 6%
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
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.

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