# Predicting Patient Response to Cancer Immunotherapy Using Quantitative Computed Tomography Based Texture Analysis

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## Abstract


- Immunotherapies are at the forefront of novel oncologic therapies, specifically inhibitors of the PD-L1/PD-1 pathway, but can be costly and toxic to patients.
- We examined if quantitative texture analysis (QTA) of baseline diagnostic CT scans could serve as a predictive biomarker for treatment response to PD-L1/PD-1
- Diagnostic CT scans of the chest, abdomen, and pelvis
- For lung lesions, mean pixel density was predictive of response (Mann-Whitney Z = 2.6, p = 0.0092 at a threshold of mean pixel density of 11.92 p < 0.0001 )
- Although a universal predictive biomarker was not found for all lesions, there was a significant difference in texture analysis of lung metastases.


## Introduction

- QTA is a novel imaging technique that evaluates lesions based on tumor heterogeneity and creates histogram data based on skewness, kurtosis, mean pixel density, entropy, mean positive pixels, and standard deviation.
- PD-L1 is often expressed on tumor cells
- PD-L1 inactivates cytotoxic T-cells (CTL) by binding PD-1, which if found on the CTL surface
- Blocking this pathway would dampen the inhibitory effect
- PD-L1/PD-1 inhibitors are associated with significant gastrointestinal and endocrine side effects
- Biomarkers serve to minimize side effects, invasive procedures, and optimize treatment strategies.
- We hypothesize that QTA would uncover a predictive biomarker for immunotherapy response

## Methods

- 20 patients, 10 responders, 10 non-responders based on RECIST criteria
- Variety of primary malignancies and previous treatments
- CT scans of chest/abdomen/pelvis acquired from Honor Health and Scottsdale Medical Imaging
- Regions of interest were placed around each lesion
- Spatial scale factors of 0-6 pixels were used to filter the images
- Histograms are developed from the filtered data based on a number of measures.

| | | Sex | Age at time of Scan | Primary Malignancy | Previous Treatment |
|---|---|---|---|---|---|
| Non-responders | 1 | F | 44 | Ovarian | Y |
| | 2 | F | 60 | Pancreas | Y |
| | 3 | M | 84 | NSCLC | Y |
| | 4 | M | 59 | NSCLC | Y |
| | 5 | M | 57 | NSCLC | Y |
| | 6 | M | 70 | NSCLC | Y |
| | 7 | F | 51 | Urothelial | Y |
| | 8 | F | 49 | Cervical | Y |
| | 9 | F | 45 | NSCLC | Y |
| | 10 | F | 67 | Urothelial | Y |
| Responders | 1 | M | 73 | NSCLC | Y |
| | 2 | M | 76 | RCC | Y |
| | 3 | M | 56 | RCC | Y |
| | 4 | F | 64 | Breast | Y |
| | 5 | F | 72 | NSCLC | Y |
| | 6 | M | 59 | RCC | Y |
| | 7 | M | 65 | Urothelial | Y |
| | 8 | M | 65 | Urothelial | Y |
| | 9 | M | 79 | Urothelial | Y |
| | 10 | M | 58 | NSCLC | Y |

*Table 1: Demographic data of responders vs. non-responders, including age, gender, primary malignancy, and if they had undergone previous treatment*

| Variable | Definition |
|---|---|
| Mean Pixel Value | Measure of average brightness |
| Kurtosis | Measure of peakedness and tailness |
| Skewness | Measure of asymmetry of histogram |
| Standard Deviation | Measure of deviation from the mean |

*Table 2: Definitions for the variables that were examined during the QTA of CT scans*

## Results

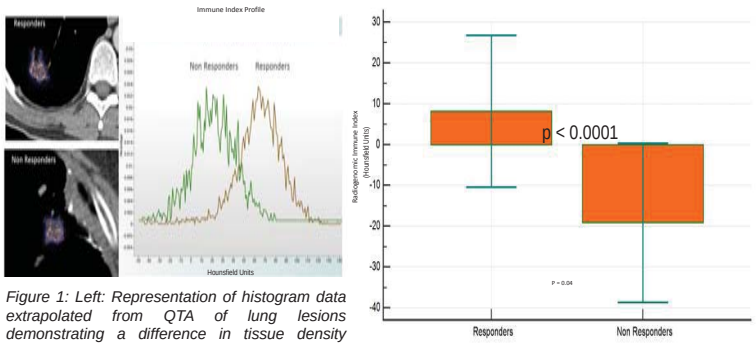


*Figure 1: Left: Representation of histogram data extrapolated from QTA of lung lesions demonstrating a difference in tissue density between responders and non-responders Right: Lung lesions examined at SSF3 based on tissue density.*

| | | Parameter | | | | | |
|---|---|---|---|---|---|---|---|
| | | Mean | SD | Entropy | MPP | Skewness | Kurtosis |
| Non-Responders | SSF 0 | 48.884 | 29.520 | 4.486 | 53.535 | 0.312 | 4.097 |
| | SSF 2 | -13.273 | 41.692 | 4.471 | 28.694 | 0.143 | 0.801 |
| | SSF 3 | -11.214 | 31.332 | 4.138 | 22.894 | 0.174 | 0.410 |
| | SSF 4 | -14.566 | 25.409 | 3.924 | 20.467 | 0.257 | 0.751 |
| | SSF 5 | -14.547 | 22.078 | 3.509 | 19.658 | -14.547 | 0.043 |
| | SSF 6 | -8.938 | 25.431 | 3.727 | 21.566 | 0.268 | -0.187 |
| | | Parameter | | | | | |
| | | Mean | SD | Entropy | MPP | Skewness | Kurtosis |
| Responders | SSF 0 | 56.378 | 26.992 | 4.478 | 59.449 | -0.471 | 1.024 |
| | SSF 2 | 1.489 | 45.718 | 4.656 | 37.624 | 0.039 | 0.511 |
| | SSF 3 | -0.916 | 31.821 | 4.157 | 26.888 | 0.003 | 0.099 |
| | SSF 4 | 8.481 | 28.017 | 4.142 | 28.792 | -0.074 | 0.466 |
| | SSF 5 | 24.785 | 22.296 | 3.688 | 35.260 | -0.182 | 0.190 |
| | SSF 6 | 32.061 | 21.312 | 3.631 | 43.001 | -0.217 | -0.036 |

*Table 3: Average compilation of data for responders vs. non-responders at all of the spatial scale factors that were used to filter the CT images. Each histogram for each SSF was examined by mean, standard deviation, entropy, mean positive pixels (MPP), skewness, and kurtosis.*

## Discussion and Conclusions

- Immunotherapies are critical for cancer treatment and cure; we hypothesize that were would be a tumor pattern that would be predictive of response
- Using QTA of lung lesions (n=14) we found that the mean pixel density at SSF3 was highly predictive of response with a threshold of 11.91 (p < 0.0001), Mann-Whitney Z statistic of 2.6 (p = 0.0092).
- Further investigation is warranted with a larger sample size separated by tumor type and potentially previous treatment.

## Acknowledgements

I wish to thank my mentor Dr. Ron Korn for his guidance and support during this project.