Simulating the impact of targeted ablation of progressive disease inmCRPC patients using machine learning

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INTRODUCTION

Treatment response heterogeneity is common in patients with metastatic cancer. In previous studies, we have shown that a substantial number of metastatic lesions continue to benefit from systemic therapy beyond biochemical or radiographic progression, and that oligo-resistant was often observed [1]. This investigation simulated the impact of targeted ablation of resistant lesions in metastatic prostate cancer (mPC) patients using artificial intelligence models.

MATERIALS AND METHODS

- ^{18}F-NaF PET/CT imaging, at baseline and on treatment, and progression-free survival (PFS) data from 118 patients with mPC from four separate prospective clinical trials were collected retrospectively.
- TRAQinform IQ technology (AIQ Solutions, Madison, WI) was used to identify, delineate, and track individual regions of interest (ROI) from baseline to follow-up.
  - Each ROI was categorized as new, increasing, stable, decreasing, or disappeared.
  - 88 imaging features were extracted from each patient (including SUV_{max}, SUV_{peak}, SUV_{totab} and intra-patient heterogeneity features)
- The TRAQinform Profile was defined as the output of random survival forest models are trained to predict progression-free survival in each cancer type, evaluated with leave-one-out cross validation
- For each patient, the largest five increasing or new ROI were simulated as lesions that had been treated with radiation therapy.
- The TRAQinform Profile was used to generate a risk score and to predict 12 month progression-free survival with and without simulated radiation therapy.
- The risk score was evaluated using the c-index and the impact of the ablation was assessed using the change in predicted PFS and odds of PFS over a year.

RESULTS

- TRAQinform IQ identified 99/118 (84%) patients that had at least one ROI that was identified as new or increasing, and 50/118 (42%) that had at least 5 new or increasing ROIs. (Figure 1)
- TRAQinform Profile score was a strong predictor of PFS with a c-index of 0.83 across all patients. (Figure 2)
- 63/118 (53%) patients were identified to have an improvement in predicted PFS (mean: 143 days, range: 2-728 days) after simulated radiotherapy of resistant lesions.
- Simulated ablation of the 5 largest increasing or new ROI resulted in an increase of the likelihood patients would reach one year before failing on treatment (mean: 14%, range: -2 to 54%). (Figure 3)

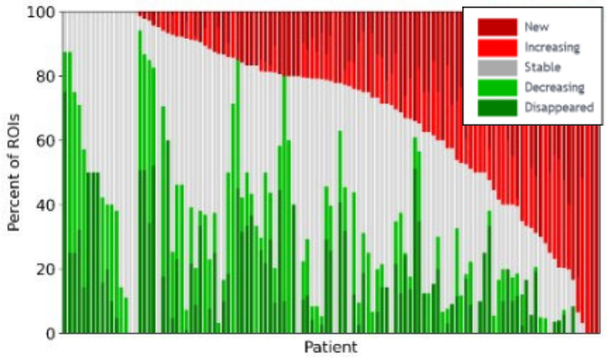

Figure 1: Heterogeneity plot of the patient population. Each column represents a patient, showing the percent of ROI for each patient that are new, increasing, stable, decreasing, or disappeared

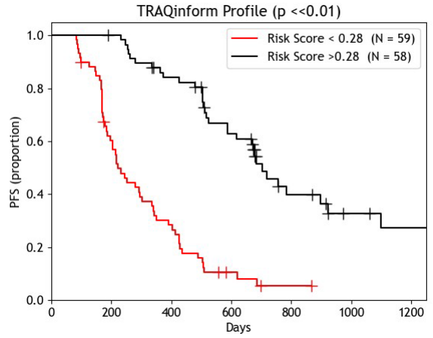

Figure 2: Kaplan-Meier curve of progression free survival, split at the median TRAQinform Profile risk score from leave-one-out cross validation

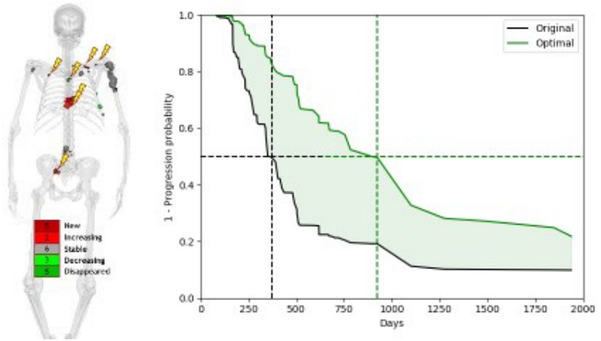

Figure 3: Example patient where simulation of a combination of 5 ROI improved the predicted time to 50% probability of progression increases from 372 to 923 days

DISCUSSION

TRAQinform Profile had a high predictive power of PFS in these patients.

TRAQinform IQ was able to identify candidate ROI for SBRT that would increase the average predicted PFS by at least 100 days as determined by TRAQinform Profile.

Further investigation of targeted ablation of oligoprogression is warranted as this simulation identified a predicted benefit for delaying PFS by a mean of 143 days.

DISCLOSURES

GL and RJ are cofounders of AIQ Solutions.

TP is employed by AIQ Solutions.

REFERENCES

[1] Christos E. Kyriakopoulos et al., Exploring Spatial-Temporal Changes in 18F-Sodium Fluoride PET/CT and Circulating Tumor Cells in Metastatic Castration-Resistant Prostate Cancer Treated With Enzalutamide. JCO 38, 3662-3671(2020). DOI:10.1200/JCO.20.00348

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