Background: Radiomics converts medical images into quantitative features and has potential in development of non-invasive biomarkers for cancer treatment. Radiomic models have not been described for ipilimumab+nivolumab (I+N) on a patient level or on an organ-specific level.

Methods: The Hillman Cancer Center registry (2015-2020) was queried for patients with melanoma treated with I+N. Clinical data was abstracted and radiographic outcomes were calculated by RECIST as well as organ-specific response. Lesions were segmented into discrete volumes-of-interest (VOI) with 400 radiomics texture features extracted. Feature filtering and selection were performed in training set independent of test set after proper normalization. XGBoost was used to construct machine learning models to predict patient level response with training/test split and 5-fold cross validation, or LOOCV in the case of organ-specific models.

Results: Of 1106 patients with melanoma, 95 were treated with I+N with 276 individual metastases. Baseline demographics included 47% female, median age of 59, 83% cutaneous (4% uveal), 51% BRAF mutant, 27% M1c (visceral non-lung), and 43% M1d (brain). Patients had a median baseline eosinophil count of 134, neutrophil-to-lymphocyte ratio (NLR) 3.29, and 78% had elevated LDH. 39% had response (CR+PR+SD) and 57% had PD, with mixed response patterns being reported more frequently in PD. Among responders, lung metastases experienced the greatest median reduction in size (-71%) whereas lymph nodes displayed the least regression (-43%). Conversely, liver metastases experienced the greatest median progression in non-responders (+39%). For patients with multiple same-organ target lesions, liver demonstrated the highest inter-lesion heterogeneity. Of the 95 patients, 84 with high-quality images were kept for radiomics model construction. XGBoost models consisting of a 16-feature radiomic signature successfully classified responders from non-responders with an AUC of 0.72. Integration of clinical variables (Age, BMI, Sex, AJCC stage M category, BRAF status, pre-treatment eosinophil, LDH, NLR) to the radiomic signature achieved an AUC of 0.87 (p=0.027). Organ-specific predictive models demonstrated similar performance as the overall response models, for example an AUC of 0.74 in lymph nodes (43 lesions) and 0.77 for liver metastases (22 lesions).

Conclusions: In this population of high-risk patients with metastatic melanoma (due to high levels of hepatic/brain involvement and non-cutaneous histology), differential organ-specific response was observed with the greatest benefit in lung, least benefit in hepatic metastases, and highest within-organ heterogeneity in liver. Integrating clinical factors with radiomics signatures improved overall response prediction suggesting priority development of these models for immunotherapy.

Ethics Approval: UPitt STUDY20020107