Background

- ¹⁸F-FDG PET/CT scans are used to assess tumor response for patients undergoing immunotherapy for metastatic melanoma. Evaluating the relationship between features derived from quantitative medical image analysis and markers in blood samples such as circulating tumor DNA (ctDNA) may present an opportunity to discover imaging and blood biomarkers that can influence future patient care.
- This study evaluates the correlation of ctDNA and radiographic imaging features derived from ¹⁸F-FDG PET/CT.

Methods

- Whole-body ¹⁸F-FDG PET/CT scans from patients with metastatic melanoma between 2014-2020 were retrospectively collected under an IRB-approved protocol.
- Patients received pembrolizumab (n=20), ipilimumab (n=4), nivolumab (n=7), or a combination of ipilimumab and nivolumab (n=19).
- TRAQinform IQ software (AIQ Solutions) (Figure 1) identified and quantified regions of interest suspicious of cancer (lesion-ROI), extracting imaging features including SUV_{max}, SUV_{mean}, and SUV_{total} in baseline (BL) and follow-up (FU) images and the change BL to FU.



Figure 1. Illustration of TRAQinform IQ analysis process.

- Plasma ctDNA concentration (copies/ml) and frequency abundance (FA) were evaluated for the first sample (1) after immunotherapy had started (between baseline and first on-treatment scan), and the next available sample (2).
- Patients were further grouped by ctDNA mutation for analysis.
- Correlation between imaging features and ctDNA features was assessed using Spearman coefficient (p).

Correlation of ctDNA and radiographic imaging features derived from ¹⁸F-FDG PET/CT for patients with metastatic melanoma treated with immunotherapy

Correlations: All mutations (N - 51) *n<0.05 **n<0.001

BL SUV _{max} -	0.47**	0.37*	-0.09	0.49**	0.37*	-0.04				
FU SUV _{max} -	0.07	0.29*	0.21	0.11	0.27	0.19				
SUV _{max} change -	-0.2	0.14	0.33*	-0.19	0.12	0.26				
BL SUV _{mean} -	0.36*	0.34*	0.04	0.38*	0.34*	0.04				
FU SUV _{mean} -	0.19	0.34*	0.15	0.22	0.32*	0.1				
SUV _{mean} change -	-0.01	0.19	0.12	0.0	0.18	0.1				
BL SUV _{total} -	0.4*	0.36*	0.01	0.41*	0.36*	0.01				
FU SUV _{total} -	-0.01	0.26	0.31*	0.01	0.23	0.27				
SUV _{tota/} change -	-0.25	0.07	0.36*	-0.24	0.06	0.29*				

ctDNA copies/ml

	ctDNA copies/ml1	ctDNA copies/ml ₂	ctDNA copies/ml	ctDNA FA1	ctDNA FA2	ctDNA FÅ change	
SUV _{total} change -	-0.19	-0.01	0.24	-0.16	-0.03	0.2	- ,
FU SUV _{total} -	0.02	0.21	0.3	0.05	0.2	0.35	
BL SUV _{total} -	0.4*	0.42*	0.02	0.4*	0.43*	0.14	
SUV _{mean} change -	0.09	0.29	0.09	0.13	0.28	0.08	- ,
FU SUV _{mean} -	0.26	0.32	0.04	0.3	0.3	0.05	- (
BL SUV _{mean} -	0.36*	0.23	-0.11	0.34	0.22	-0.06	-
SUV _{max} change -	-0.12	0.19	0.32	-0.09	0.16	0.25	- (
FU SUV _{max} -	0.14	0.31	0.19	0.19	0.29	0.21	- (
BL SUV _{max} -	0.49*	0.31	-0.23	0.5*	0.32	-0.11	-

Figure 2. Heatmaps displaying the Spearman Correlation coefficients for all feature combinations.

CONFLICT OF INTEREST: OL and TP are employed by AIQ Solutions (Madison, WI, USA). AIQ Solutions and UWA have established a collaborative, full-time research fellowship in medical imaging. MD holds one of these AIQ Solutions Fellowships.

Spearman Correlations: BRAF mutations (N = 32) *p<0.05, **p<0.001

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Results

- 0.8

-0.6

-0.4

-0.2

-0.0

- -0.2

-0.4

- -0.6

- -0.8

ρ

DNA FA change

- (range 23 83).

- correlations.

Conclusion

This study shows that in patients with metastatic melanoma receiving immunotherapy, quantitative features from blood biomarkers such as ctDNA correlate with ¹⁸F-FDG PET/CT imaging features. Combining blood biomarkers with imaging strengthen are spatially localizable teatures that prognostication in this patient group. Further analysis is being performed with additional types of ctDNA mutations.



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Patient characteristics: 32 males and 19 females with average age of 62 years

For all 51 patients, a moderate correlation was observed between SUV_{max,BI} and ctDNA copies/ml₁ (ρ = 0.47, p<< 0.001), SUV_{max.BL} and ctDNA FA₁ (ρ = 0.49, p << 0.001), and between SUV_{total.BL} and ctDNA FA₁ (ρ = 0.41, p < 0.0024).

In BRAF mutation patients (N=32), moderate correlations existed between SUV_{max.BL} with ctDNA copies/ml₁ (ρ = 0.49, p = 0.0041 and ctDNA FA1 (ρ = 0.5, p = 0.0035), and SUV_{total BI} with ctDNA copies/ml₂ ($\rho = 0.42$, p = 0.017), ctDNA FA₁ ($\rho =$ 0.40, p = 0.023), and ctDNA FA₂ (ρ = 0.43, p = 0.015).

All the other combinations displayed weak ($\rho < 0.39$) or non-significant ($\rho > 0.05$)

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