

CORRELATION OF CTDNA WITH ORGAN- AND BONE-SPECIFIC RADIOGRAPHIC IMAGING FEATURES DERIVED FROM ¹⁸F-FDG PET/CT FOR PATIENTS WITH METASTATIC MELANOMA TREATED WITH IMMUNOTHERAPY

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Background

Plasma circulating tumour DNA (ctDNA) can provide real-time information about disease status in patients with metastatic melanoma (MM). After initial staging ¹⁸F-FDG PET/CT scans, regular interval scans are performed to continue assessing ongoing response to systemic therapies such as immunotherapy. Combining blood biomarkers with the radiographic features extracted from scans provides an opportunity to discover non-invasive indicators and potentially leads to more tailored treatment strategies for patients with advanced melanoma. This study aimed to investigate the correlation of ctDNA concentration and application of automated radiographic imaging feature extraction of organ- and bone-specific disease from ¹⁸F-FDG PET/CT for patients with MM treated with immunotherapy.

Methods

Forty-seven patients received pembrolizumab (n=17), ipilimumab (n=4), nivolumab (n=6), or a combination of ipilimumab and nivolumab (n=20) between 2014-2020. Whole-body Baseline (BL) and follow-up (FU) ¹⁸F-FDG PET/CT scans were retrospectively collected under IRB-approved protocol. TRAQinform IQ software (AIQ Solutions) identified and quantified regions of interest suspicious of cancer (lesion-ROI), enabling extraction of imaging features including SUVtotal, SUVmax, SUVmean, and volume of organ- and bone-specific lesion-ROI. 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). Correlation between imaging features was assessed using Spearman coefficient (ρ).

Results

	ctDNA copies/ml1	ctDNA copies/ml2	ctDNA copies/ml	ctDNA FA1	ctDNA FA2	ctDNA FÅ change	
SPINE FU SUV _{mean} -	-0.0	0.44*	0.46*	-0.01	0.44*	0.54**	
SPINE FU SUVtotal	-0.01	0.43*	0.44*	-0.02	0.43*	0.54**	
SPINE FU SUVmax	0.01	0.45*	0.45*	0.0	0.45*	0.54**	
SPINE BL SUVmean	0.22	0.17	-0.04	0.26	0.18	0.08	
SPINE BL SUV	0.22	0.16	-0.04	0.25	0.17	0.09	
SPINE BL SUV	0.23	0.17	-0.04	0.26	0.18	0.09	
RIBS FU SUV	0.05	0.21	0.13	0.06	0.21	0.14	
RIBS FU SUV	0.05	0.21	0.13	0.06	0.21	0.13	
RIBS FU SUV	0.06	0.21	0.12	0.07	0.22	0.13	
RIBS BL SUV	0.53**	0.27	-0.19	0.51**	0.24	-0.2	
RIBS BL SUV	0.54**	0.27	-0.2	0.51**	0.25	-0.18	
RIBS BL SUV	0.54**	0.28	-0.19	0.52**	0.25	-0.18	
UNGS FU SUV	0.16	0.19	0.01	0.2	0.21	0.11	
	0.06	0.13	0.06	0.1	0.15	0.17	
	0.13	0.17	0.04	0.17	0.2	0.14	- 0,
	0.05	0.01	-0.05	0.07	0.01	0.06	
	0.05	0.02	-0.04	0.06	0.01	0.07	
LUNGS BL SUV	0.07	0.01	-0.06	0.09	0.0	0.05	0.
	0.18	0.31*	0.14	0.19	0.29*	0.01	- 0
	0.17	0.32*	0.16	0.18	0.3*	0.03	
LIVER FILSUV	0.17	0.32*	0.15	0.19	0.31*	0.03	
	0.28	0.31*	0.01	0.27	0.3*	-0.04	- 0,
	0.24	0.3*	0.03	0.24	0.28	-0.02	
	0.24	0.32*	0.06	0.25	0.31*	0.01	
	0.14	0.20	0.17	0.14	0.20	0.10	- 0,
DOWEL FU SUVmax	0.1/	0.31*	0.19	0.16	0.31*	0.19	
BOWEL BL SUVmean	0.13	0.24	0.02	0.09	0.20	0.05	
SOWEL BL SUV	0.13	0.23	0.03	0.08	0.20	0.04	U
BOWEL BL SUV _{max}	0.13	0.24	0.02	0.09	0.27	0.03	- 0
	0.12		0.00		0.07	0.07	
		Spearman (Correlations: All m	utations *p<0.05	, **p<0.001		

The median age at the time of immunotherapy was 62 (range; 23-83) and 48% of patients were male. For all 47 patients, moderate correlation was observed for lesion-ROI in the bones compared to ctDNA. For ribs, the SUVtotal,BL with ctDNA copies/ml1 (ρ = 0.54, p<< 0.001) and ctDNA copies/FA1 (ρ = 0.51, p = p<< 0.001). For spine, SUVtotal,FU with ctDNA copies/ml2 (ρ = 0.43, p = 0.002) and ctDNA copies/FA2 (ρ = 0.53, p<< 0.001).

Figure 1. Heatmap displaying the Spearman Correlation coefficients for feature combinations.

Conclusion

This study demonstrates moderate correlation between ctDNA concentrations and radiographic imaging features in patients with MM undergoing immunotherapy. The findings support the potential of ctDNA as a valuable biomarker for identifying organ- and bone-specific tumor burden, enhancing the precision of non-invasive disease monitoring. The integration of automated radiographic feature extraction with ctDNA analysis could improve the accuracy of tumor metabolic behavior assessments. Further research is warranted to validate these findings and explore additional biomarker combinations for comprehensive disease monitoring.

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Figure 2. Response map of a patient with high frequency of new lesion-ROI observed.