Application of novel machine learning to predict immunotherapy related toxicities for metastatic melanoma patients from baseline and follow up ^{18}F-FDG PET/CT scans

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Background

- Immune checkpoint inhibitors have been shown to provide durable responses in metastatic melanoma (MM) patients, however, immune-related adverse events (irAE) are frequently experienced and can be challenging to manage.
- ^{18}F-FDG PET/CT medical imaging, has the potential to predict both tumour response and irAE non-invasively [1].
- Opportunities to predict toxicity and influence clinical care are presented via quantification of features derived from medical images using machine learning models [2].
- This study implements automated organ segmentation and machine learning (ML) using ^{18}F-FDG PET/CT images to predict irAE for patients with MM.

Methods

- 216 ^{18}F-FDG PET/CT scans taken between 2013-2021 for 108 patients with MM treated with immunotherapy were retrospectively collected.
- Organs in Table 1 were segmented automatically on the CT using AIQ Solutions technology (Figure 1).
- Segmented organs were used to quantify uptake and correlate with Grade ≥ 2 irAE. If patients experienced more than one event the first was included for analysis.
- Imaging features were extracted from organs pre-immunotherapy at baseline (BL) and first follow-up (FU).
- Organ uptake and changes across time were evaluated for predicting irAE using univariate receiver operating curve (ROC) analysis and a random forest model was trained using 10-fold cross-validation to predict occurrence of irAE.
- Performance was evaluated using area under the ROC (AUROC).

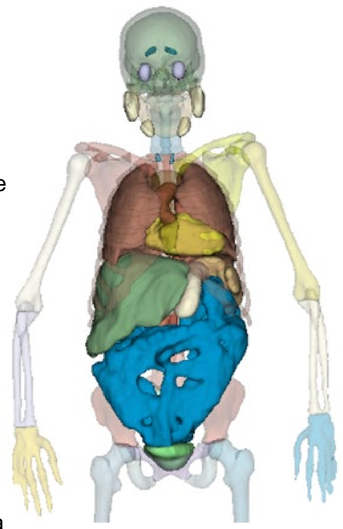
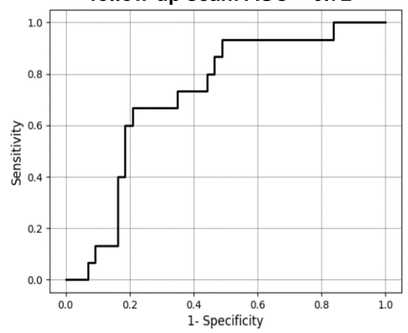


Figure 1. *Organ segmentation.*

Predicting irAE from baseline and follow-up scan: AUC = 0.72



Individual 'score' predicting any toxicity from baseline and follow-up scan

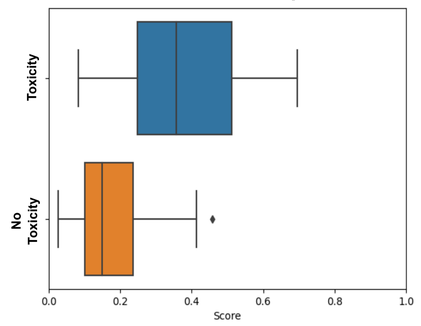


Figure 2. *Left; AUROC of random forest plot predicting any toxicity from BL and FU scans. Right; Box plot demonstrating distribution of patients individual scores.*

AUROC for prediction of any irAE based on the BL and first FU scan was 0.72 (Figure 2). Change in 75th percentile of SUVs ($SUV_{75\%}$) in FU was predictive of irAE in thyroid (AUC=0.87) and bowel (AUC=0.82) (Table 2).

Table 1. *Number and type of irAE.*

Organ	Immune-related Adverse Events	N
Adrenals	Adrenal insufficiency	3
Liver	Alanine aminotransferase increase	13
Bowel	Colitis/Diarrhea	21
Thyroid	Thyroid dysfunction	10
Pituitary gland	Hypophysitis	6
Pancreas	Lipase increased	2
Pancreas	Pancreatitis	3
Lung	Pneumonitis	4

Patient characteristics:

- 71 males and 37 females
- Average age 62 (range 23-88)
- **62 patients with irAE** grouped per organ for univariate analysis (42 patients were control cohort)
- There was high frequency of thyroid dysfunction, raised alanine aminotransferase and colitis/diarrhea

CONFLICT OF INTEREST: DH, RMG, and TP are employed by AIQ Solutions (Madison, WI, USA). AIQ Australia Pty Ltd in collaboration with UWA have established AIQ Research Fellows - full time research fellowships in medical imaging. Dr Dell'Oro holds one of these Fellowships.

Results

Table 2. *ROC analysis per irAE with the highest frequency.*

Immune-related Adverse Events	Scan	Measure	AUC
Alanine aminotransferase increase	BL	$SUV_{75\%}$	0.61
Colitis/Diarrhea	FU	$SUV_{75\%}$	0.82
Thyroid dysfunction	FU	$SUV_{75\%}$	0.87

Conclusion

Our results indicate quantitative features from ^{18}F-FDG PET/CT imaging using metrics from the baseline and follow up scans may be used to evaluate irAE in metastatic melanoma patients receiving immunotherapy. A machine learning score was developed to evaluate features that may predict risk of toxicity in the form of a single patient-level metric. This warrants further investigation in a prospective setting.

References

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