AI-assisted whole-body assessment of immunotherapy response using [18F]F-AraG, a PET agent for activated T cells

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Background

[18F]F-AraG is a PET agent for imaging activated T cells, that has shown promise in providing early indication of response to T cell mediated therapies (Fig. 1A). Whole body assessment of [18F]F-AraG scans may provide analysis of systemic immunologic processes and allow a more comprehensive evaluation of response to immunotherapies. Here, we employ AIQ Solutions' TRAQinform IQ technology [Fig. 1B], to create [18F]F-AraG-based response maps for head and neck squamous cell carcinoma (HNSCC) patients undergoing anti-PD-1 therapy.

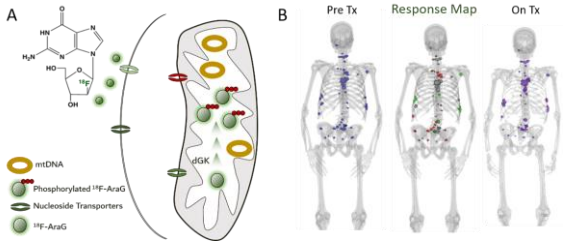

Figure 1. A. Phosphorylation of [18F]F-AraG by mitochondrial deoxyguanosine kinase (dGK) leads to entrapment and potential downstream accumulation into mtDNA. In response to activation T cells undergo metabolic reprogramming and dramatically increase both mitochondrial mass and mtDNA which can be visualized by [18F]F-AraG. **B.** Using TRAQinfrom IQ technology, images are uploaded into the cloud; lesions are identified and classified as benign or malignant on each patient scans. Articulated registration is used to match lesions and changes in lesion uptake is used to sort them into response categories.

Methods

Four treatment-naïve HNSCC patients were imaged using [18F]F-AraG before and 2-3 weeks after a single dose of anti-PD-1 antibody (Fig. 2). Using TRAQinform IQ technology, standardized uptake values, SUV_{max}, SUV_{mean} and SUV_{total} were extracted from all areas of tracer uptake in the baseline and on-treatment scans and changes in signal calculated to assess therapy effects.

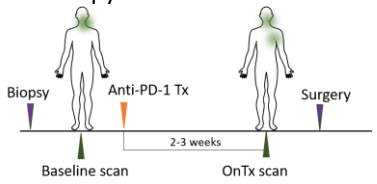

Figure 2. Study scheme

Results

1. TRAQinform IQ whole-body evaluation of [18F]F-AraG PET revealed intra and inter patient heterogeneity in the signal change post anti-PD-1 therapy (Fig.3).

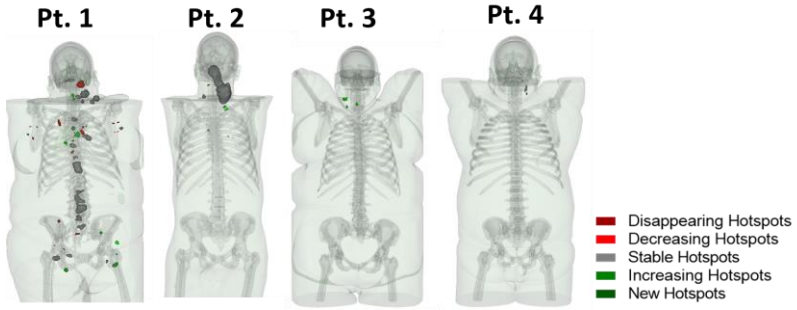

Figure3. The change in SUV mean in four head and neck patients pre and post anti-PD-1 therapy. Different colors represent positive (green), negative (red) and no change (grey) in signal post therapy.

2. In some patients, the response map differed depending on the SUV metric used, highlighting the importance of SUV metric choice in evaluating response to therapy.

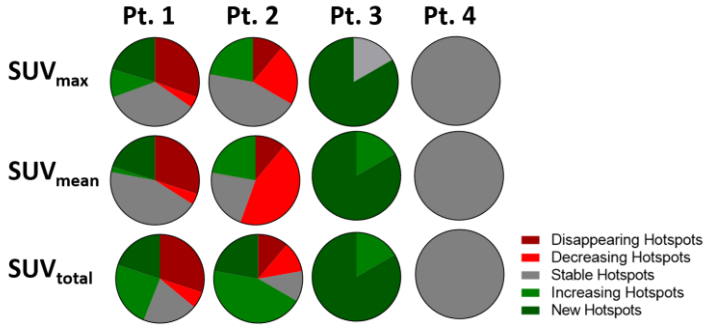

Figure 4. Intra- and inter-patient heterogeneity of the signal (SUV_{max}, SUV_{mean} and SUV_{total}) change. Pie charts represent distribution of areas with a change in [18F]F-AraG signal post therapy

3. The [18F]F-AraG signal change post anti-PD-1 therapy trended with patients' outcome. The patients with areas where the signal disappeared or decreased post therapy, indicative of the lack of T cell activation, had shorter overall survival than the patients with areas with stable and increasing signal (Fig.5).

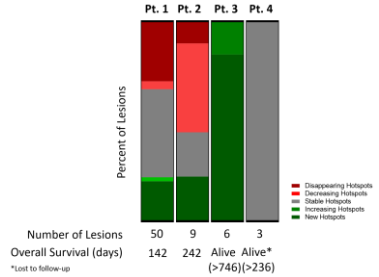

Figure5. The response maps based on the change in SUV_{mean} in four head and neck patients treated with anti-PD-1 therapy.

4. FACS analysis of the tumor samples of the patient with the shortest overall survival showed an increase in the number of CD8 cells and activation marker CD38 post anti-PD-1 injection. [18F]F-AraG-based response map shows heterogenous response throughout the body but also within the primary lesion, underscoring the shortcomings of serial biopsy and potential utility of comprehensive whole-body analysis in evaluating response to immunotherapies.

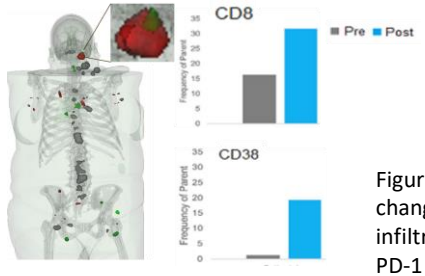

Figure6. The association between the change in SUV_{mean} and changes in T cell infiltration in the primary lesion post anti-PD-1 therapy.

Conclusions

Analysis and quantification of [18F]F-AraG PET using TRAQinform IQ technology provides patient-level assessment of all areas with tracer uptake and may allow for better understanding of heterogeneity of T cell activation and potentially offer a more comprehensive evaluation of response to immunotherapy than the standard, tumor-centric, radiologic methods.

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