Application Note:
Immunotherapy Treatment Response and Toxicity Risk

Introduction

Immunotherapy agents show great promise and are currently used to treat a growing range of cancers. However, emerging evidence from randomized trials and clinical practice demonstrate highly variable patterns of toxicity and treatment response that can lead to severe immune-related adverse events. The complex interplay between tumor response, immune-induced organ toxicity and immune system activation make a comprehensive assessment of treatment response extremely difficult.

Early identification of both the benefits and the risks associated with immunotherapy are essential for the efficient development of effective therapies and will enable investigators to differentiate between patients who are likely to have an optimal vs. a sub-optimal response to therapy. This can impact the overall clinical outcome and reduce the number of severe or life-threatening adverse events, which are critical for guiding therapeutic management in the clinical setting.

Technology Application in Immunotherapy Assessments

AIQ Solutions (AIQ) has performed two independent assessments to demonstrate how its medical device software technology platform is able to quantify and predict a patients' response to immunotherapeutic treatments, as well as their risk for toxicity.

Assessment 1 - Predicting Patient Response

Methods:

This assessment was based on a retrospective study of 15 metastatic melanoma patients treated with immune checkpoint inhibitor therapy. All patients received at least two ^{18} Fluorodeoxyglucose (FDG) Positron Emission Tomography/Computerized Tomography (PET/CT) scans during therapy. A clinical oncologist independently classified each patient as a "responder" or a "progressor" based upon a detailed review of the patient's clinical data. AIQ Treatment Response Assessments (TRA) were generated and disease burden defined as the total tracer Standard Uptake Value (SUV_{TOTAL}). For each patient, the disease burden associated with each individual lesion as well as the disease burden for all lesions, were quantified from the first (T1) and the second (T2) scans. AIQ then correlated the change in total disease burden between T1 to T2, for each patient, to the independent oncologist's previous treatment response classification.

Results:

There was a strong correlation between the change in total disease burden from T1 to T2 and the oncologist's response classifications (See Figure 1). Early change in total disease burden, as quantified by AIQ's technology platform, predicted eventual treatment response with a high degree of specificity and sensitivity (See Figure 2).

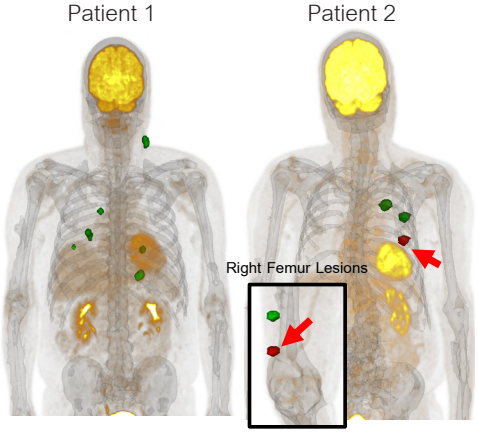

Figure 1 (Left)
TRA on two patients from PET/CT images. Patient 1 displays stronger response to immunotherapy treatment, placing that patient into the "responder" classification. Patient 2 displays weaker response to treatment and is placed into the "progressor" classification.

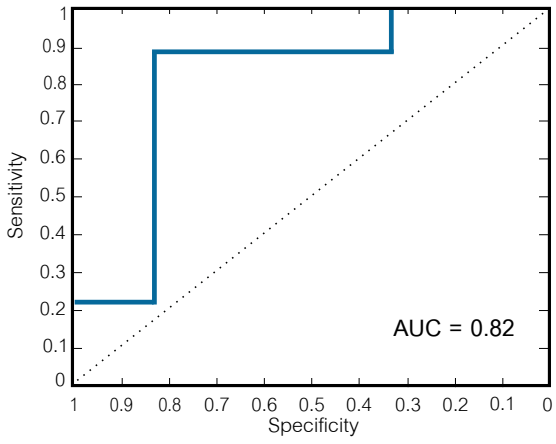

Figure 2 (Right)
Early Total Disease Burden: AIQ can predict eventual treatment response with both high sensitivity and specificity.

Assessment 2 - Predicting Patient Toxicity Risk

Methods:

This assessment was based on a retrospective study of 35 metastatic melanoma patients treated with immune checkpoint inhibitor therapy. All patients received at least three FDG PET/CT scans during therapy. AIQ's algorithm identified and segmented soft tissue organs. TRAs were generated (See Figure 3). Changes in the total FDG Standardized Update Value (SUV_{TOTAL}) were quantified in healthy organs between different timepoints T1 to T2 and T2 to T3 (T = time point in therapy when the patient received an FDG PET/CT). Change in SUV in healthy tissue was compared between patients who eventually developed colitis and those who did not. Additionally, for those patients who developed colitis, the time of the scans were compared to the initial colitis diagnosis by a clinician.

Results:

AIQ demonstrated that accurate quantification of the change in bowel FDG tracer uptake can significantly predict which patients had colitis, 50 days prior to actual diagnosis, with a high degree of specificity and sensitivity (See Figure 4). AIQ's technology platform is capable of accurately measuring subtle changes in tracer uptake in healthy tissue, to predict toxicity in vulnerable soft tissue organs.

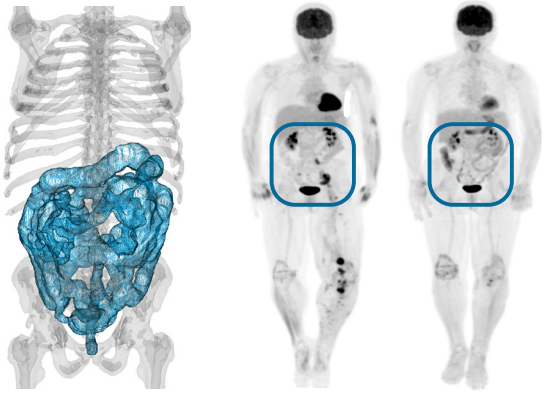

Figure 3:
TRA graphic of a patient's bowl segmentation (Left) derived from 2 PET/CT images (Right)

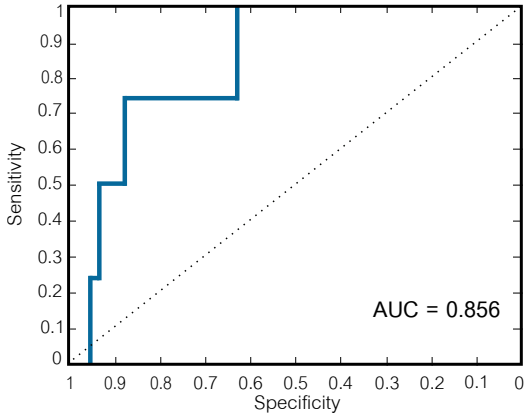

Figure 4:
Prediction of colitis with both high sensitivity and specificity.

Immunotherapy Technology Application Conclusion

The two assessments discussed above demonstrate that AIQ's technology can reliably predict both treatment response and toxicity risk during immunotherapy. In both examples, AIQ highlights the sensitivity of the technology and its ability to transform imaging metrics into intelligence that can impact patient outcomes. In the first assessment, the results demonstrate independent treatment response classifications strongly correlated to early changes in total disease burden. In the second assessment, the results demonstrate early changes in tracer uptake in healthy tissue can predict adverse events. The metastatic melanoma assessments in this application note, serve only as a proof of concept. AIQ's technology platform is adaptable and can be similarly used in other immunotherapeutic studies.

AIQ's technology provides the intelligence to help clinicians balance the complex relationship between immune response and immune-induced adverse events. This intelligence delivers actionable steps to maximize benefits and reduce risks associated with immunotherapeutics, which in turn enables stronger go/no-go decisions in early stage drug development.

About AIQ Solutions

AIQ has developed a medical device software platform that uses artificial intelligence to automatically quantify treatment response for each individual lesion from longitudinal imaging data. The platform delivers lesion-specific metrics, including spatial information; it also calculates a composite biomarker for each patient that indicates early in the course of treatment whether that patient is likely to exhibit an optimal or sub-optimal response to therapy as well as assess patient's toxicity risk.