

A COMPREHENSIVE METHODOLOGY FOR PET-BASED  
TREATMENT RESPONSE ASSESSMENT

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Assessment of treatment response is essential for disease management and can strongly influence subsequent treatment decisions. Current methodologies for PET-based assessment of treatment response are limited and fail to adequately characterize response using all available functional data. We developed a methodology for more comprehensive and robust treatment response assessment using PET imaging. The methodology examined a variety of PET imaging metrics acquired at multiple time-points over the course of therapy. PET metrics were tested for: responsiveness – the variation of a metric across all patients; uncertainty – the repeatability and sensitivity associated with a metric; association with the clinical endpoint using the Cox proportional hazards model. Candidate imaging biomarkers of treatment response (IBTR) were identified as those metrics with high responsiveness-to-uncertainty ratio and strong association with the clinical endpoint. The methodology was applied to two clinical trials involving [<sup>18</sup>F]FLT PET imaging (FLT, marker of cellular proliferation) of cancer patients receiving therapy.

**Clinical trial 1:** Seventeen patients with advanced solid malignancies were treated with molecular targeted therapy and imaged pre-, mid-, and post-treatment. Tumor size, SUV, and uptake distribution metrics were tested for responsiveness, sensitivity to different tumor segmentation techniques, and association with time to disease progression. Candidate IBTR included pre- and post-treatment  $SUV_{max}$ , post-treatment  $SUV_{peak}$ , and response difference

histograms quantifying the differences between the pre- and post-treatment as well as mid- and post-treatment uptake distributions.

**Clinical trial 2:** Seven adult patients with acute myeloid leukemia (AML) were treated with induction chemotherapy and imaged at progressively earlier time points during therapy. Total body bone marrow was characterized using  $SUV_{max}$ ,  $SUV_{peak}$ ,  $SUV_{mean}$ , an activity volume histogram, and the heterogeneity of the uptake distribution. These metrics were all candidate IBTR, as patients who entered complete remission could be distinguished from those with resistant disease, possibly as early as two days after the beginning of treatment.

Due to limited patient numbers, results of these studies are suggestive of potential candidate IBTRs warranting further investigation in larger clinical trials. Ultimately, the methodology could be used for more complete, accurate, and robust response assessment enabling clinicians to make better, more informed treatment decisions to improve clinical outcomes.

A handwritten signature in black ink, appearing to read "Q. Zeng". The signature is written in a cursive, fluid style with a large initial "Q" and a stylized "Zeng".