

**Purpose:**The accuracy of quantitative PET is influenced by many factors whose uncertainties need to be characterized for its reliable use in treatment response assessment. Among the factors are residual activity and lack of synchronization between PET-scanner and dose-calibrator clocks which are frequently overlooked. Therefore, we characterized their effects on PET-based treatment response assessment.

**Methods:**Fifteen patients receiving targeted molecular therapy underwent whole body [18F]FLT PET/CT scans at multiple time points. Response was calculated as the change in SUV between subsequent scans. Residual-activity left in syringe after injection effects were assessed by comparing response measures when SUV values were corrected for residual activity (range: 0.07mCi-0.61mCi) to when they were not. Uncertainty in response was also compared between scans where the synchronization of the PET-scanner and dose-calibrator clocks were randomly offset (range: 1min-60mins) to when they were synchronized. The effect of both factors on PERCIST classification of treatment response was assessed.

**Results:**Residual-activity and lack of clock synchronization had significant effects on treatment response ( $p=0.05$ ). 3% change in clock offsets between subsequent scans resulted in 2.5% absolute difference in response. The mean difference in responses due to desynchronized clocks was 18% (maximum=35%). 3% change in residual activity resulted in 0.1% absolute difference in response. Not accounting for residual-activity caused mean difference of 1% (maximum=6%) in the response. Changes in clock synchronization and not accounting for residual activity resulted in reclassification of the PERCIST response status of over 30% of the patients.

**Conclusions:**Lack of synchronization between PET-scanner and dose-calibrator clocks and not accounting for residual activity caused a difference in response. Administration procedures that minimize residual activity (e.g. flushing syringe with saline) have to be implemented. Also, all clocks used with dose-calibrator have to be synchronized with PET-scanner clock periodically. Otherwise patients can be wrongly classified as partial, stable, or progressive disease.