Real-Time Pharmacokinetic Analysis

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Objectives: We previously developed a photoplesthmograph (PPG) device which – operating on the same principles as a pulse oximeter - noninvasively measures the concentration of optically active materials in the bloodstream [1]. The objective of this study was to demonstrate the use of the real-time PPG concentration measurements for continuously updating individual pharmacokinetic parameter estimates during injection to make real-time predictions of individual exposure to indocyanine green (ICG).

Methods: In a secondary analysis of ICG injected into the tail of BALB/c mice, a population pharmacokinetic model was calibrated, using WinBUGS, to PPG data from 14 mice: 4, 6 and 4 mice received a low, medium, and high dose, respectively. Mice were injected at a constant rate until the desired ICG concentration was achieved with the PPG measuring the concentration every 5 seconds until the concentration returned to baseline. For validation, the individual predictions of exposure were made for 8 mice (2 low, 3 medium, and 3 large doses) where the posterior distributions from the population pharmacokinetic model were the prior parameter distributions and the individual pharmacokinetic parameter distributions – and corresponding exposure predictions – were updated in a Bayesian manner with each PPG measurement.

Results: The average absolute percent error between the individual predicted exposure and the actual exposure continuously decreased (31.7%, 23.6%, 14.2%, 11.1%, 9.8%, and 9.4%) every minute during the injection (see Figure).

![Figure 1: Absolute value of the percent error between the individual predicted exposure (AUC) and the actual exposure for each of the 8 validation mice. Model-predictions were made after every PPG measurement (every 5 seconds) during the injection of ICG.](image)

In a simulation, 9.5 minutes of PPG measurements were required for 90% confidence in the individual exposure prediction being within 10% of the actual exposure.

Conclusions: The real-time concentration measurement capabilities of the PPG enable individual predictions of exposure while a drug is being injected. For ICG, if the injection rate provides 9.5 minutes of data, the exposure can be predicted to within 10% and these model predictions could then be used to adjust the injection to ensure that the desired exposure is achieved.

References: