

***In Silico* Testing—Impact on the Progress of the Closed Loop Insulin Infusion for Critically Ill Patients Project**

Malgorzata E. Wilinska, Ph.D., Ludovic J. Chassin, Ph.D., and Roman Hovorka, Ph.D.

Abstract

Background:

In silico testing was used extensively in the European Commission-funded Closed Loop Insulin Infusion for Critically Ill Patients (Clinicip) project, which aimed to develop prototype systems for closed loop glucose control in the critically ill. This article presents two examples of how the simulation environment was utilized in this project.

Methods:

The *in silico* simulation environment was used to simulate a 48-hour clinical trial in a surgical intensive care unit to achieve tight glycemic control. A set of 10 critically ill synthetic subjects was selected for two different studies. In the first study, two sets of clinical trials were simulated using two versions of a model predictive control (MPC)-based glucose control algorithm: MPC Version 0.1.5 with hourly glucose measurements and updated MPC Version 1.4.3 with variable 1- to 4-hour glucose sampling. In the second study, four sets of clinical trials were simulated with four levels of measurement error at 2, 5, 7, and 15% coefficient of variation corresponding to the measurement error of commercially available glucose measuring devices.

Results:

In the first study, more frequent glucose measurements associated with MPC Version 0.1.5 facilitated more efficacious and safer glucose control compared to that obtained with the prolonged and variable glucose sampling rate associated with MPC Version 1.4.3. In the second study, a marked deterioration in safety measures was observed in studies performed with a measurement error of 15%.

Conclusions:

The presented simulation studies highlighted two important uses of *in silico* simulation environment in the Clinicip project. The impressive progress and successful completion of the Clinicip project would not be possible without computer-based simulations.

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Author Affiliation: Department of Pediatrics, University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom

Abbreviations: (Clinicip) Closed Loop Insulin Infusion for Critically Ill Patients, (CV) coefficient of variation, (EC) European Commission, (HGI) hyperglycemic index, (ICU) intensive care unit, (MPC) model predictive control, (SD) standard deviation, (TGC) tight glycemic control

Keywords: critical illness, glucose control, simulation environment

Corresponding Author: Malgorzata E. Wilinska, Ph.D., Department of Pediatrics, University of Cambridge, Level 8, Addenbrooke's Hospital, Hills Road, Box 116, Cambridge CB2 0QQ, UK; email address mew37@cam.ac.uk