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SYMPOSIUM

Continuous Glucose Monitoring Considerations for the Development of a Closed-Loop Artificial Pancreas System

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Abstract

Background:

Commercialization of a closed-loop artificial pancreas system that employs continuous subcutaneous insulin infusion and interstitial fluid glucose sensing has been encumbered by state-of-the-art technology. Continuous glucose monitoring (CGM) devices with improved accuracy could significantly advance development efforts. However, the current accuracy of CGM devices might be adequate for closed-loop control.

Methods:

The influence that known CGM limitations have on closed-loop control was investigated by integrating sources of sensor inaccuracy with the University of Virginia Padova Diabetes simulator. Non-glucose interference, physiological time lag and sensor error measurements, selected from 83 Enlite™ glucose sensor recordings with the Guardian® REAL-Time system, were used to modulate simulated plasma glucose signals. The effect of sensor accuracy on closed-loop controller performance was evaluated *in silico*, and contrasted with closed-loop clinical studies during the nocturnal control period.

Results:

Based on n = 2472 reference points, a mean sensor error of 14% with physiological time lags of 3.28 ± 4.62 min (max 13.2 min) was calculated for simulation. Sensor bias reduced time in target for both simulation and clinical experiments. In simulation, additive error increased time <70 mg/dl and >180 mg/dl by 0.2% and 5.6%, respectively. In-clinic, the greatest low blood glucose index values (max = 5.9) corresponded to sensor performance.

Conclusion:

Sensors have sufficient accuracy for closed-loop control, however, algorithms are necessary to effectively calibrate and detect erroneous calibrations and failing sensors. Clinical closed-loop data suggest that control with a higher target of 140 mg/dl during the nocturnal period could significantly reduce the risk for hypoglycemia.

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Abbreviations: (A1c) hemoglobin A1c., (AP) artificial pancreas, (BG) blood glucose, (CF) calibration factor, (CGM) continuous glucose monitoring, (CSII) continuous subcutaneous insulin infusion, (ePID) external physiologic insulin delivery, (FDA) Food and Drug Administration, (HBGI) high blood glucose index, (ISF) interstitial fluid, (LBGI) low blood glucose, (MARD) mean absolute relative difference, (SMBG) self-monitoring of blood glucose, (UVa) University of Virginia

Keywords: artificial pancreas, closed loop, continuous glucose monitoring, glucose sensor, hypoglycemia, insulin pump

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