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ORIGINAL ARTICLES

Multinational Study of Subcutaneous Model-Predictive Closed-Loop Control in Type 1 Diabetes Mellitus: Summary of the Results

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Abstract

Background:

In 2008–2009, the first multinational study was completed comparing closed-loop control (artificial pancreas) to state-of-the-art open-loop therapy in adults with type 1 diabetes mellitus (T1DM).

Methods:

The design of the control algorithm was done entirely *in silico*, i.e., using computer simulation experiments with $N = 300$ synthetic "subjects" with T1DM instead of traditional animal trials. The clinical experiments recruited 20 adults with T1DM at the Universities of Virginia (11); Padova, Italy (6); and Montpellier, France (3). Open-loop and closed-loop admission was scheduled 3–4 weeks apart, continued for 22 h (14.5 h of which were in closed loop), and used a continuous glucose monitor and an insulin pump. The only difference between the two sessions was that insulin dosing was performed by the patient under a physician's supervision during open loop, whereas insulin dosing was performed by a control algorithm during closed loop.

Results:

In silico design resulted in rapid (less than 6 months compared to years of animal trials) and cost-effective system development, testing, and regulatory approvals in the United States, Italy, and France. In the clinic, compared to open-loop, closed-loop control reduced nocturnal hypoglycemia (blood glucose below 3.9 mmol/liter) from 23 to 5 episodes ($p < .01$) and increased the amount of time spent overnight within the target range (3.9 to 7.8 mmol/liter) from 64% to 78% ($p = .03$).

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Abbreviations: (CGM) continuous glucose monitoring, (FDA) Food and Drug Administration, (IV) intravenous, (MPC) model-predictive control, (SC) subcutaneous, (T1DM) type 1 diabetes mellitus

Keywords: closed-loop control, continuous glucose monitoring, type 1 diabetes mellitus

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Abstract cont.

Conclusions:

In silico experiments can be used as viable alternatives to animal trials for the preclinical testing of insulin treatment strategies. Compared to open-loop treatment under identical conditions, closed-loop control improves the overnight regulation of diabetes.

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