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ORIGINAL ARTICLE

# Model-Based Closed-Loop Glucose Control in Type 1 Diabetes: The DiaCon Experience

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## Abstract

### *Background:*

To improve type 1 diabetes mellitus (T1DM) management, we developed a model predictive control (MPC) algorithm for closed-loop (CL) glucose control based on a linear second-order deterministic-stochastic model. The deterministic part of the model is specified by three patient-specific parameters: insulin sensitivity factor, insulin action time, and basal insulin infusion rate. The stochastic part is identical for all patients but identified from data from a single patient. Results of the first clinical feasibility test of the algorithm are presented.

### *Methods:*

We conducted two randomized crossover studies. Study 1 compared CL with open-loop (OL) control. Study 2 compared glucose control after CL initiation in the euglycemic (CL-Eu) and hyperglycemic (CL-Hyper) ranges, respectively. Patients were studied from 22:00–07:00 on two separate nights.

### *Results:*

Each study included six T1DM patients (hemoglobin A1c 7.2% ± 0.4%). In study 1, hypoglycemic events (plasma glucose < 54 mg/dl) occurred on two OL and one CL nights. Average glucose from 22:00–07:00 was 90 mg/dl [74–146 mg/dl; median (interquartile range)] during OL and 108 mg/dl (101–128 mg/dl) during CL (determined by continuous glucose monitoring). However, median time spent in the range 70–144 mg/dl was 67.9% (3.0–73.3%) during OL and 80.8% (70.5–89.7%) during CL. In study 2, there was one episode of hypoglycemia with plasma glucose <54 mg/dl in a CL-Eu night. Mean glucose from 22:00–07:00 and time spent in the range 70–144 mg/dl were 121 mg/dl (117–133 mg/dl) and 69.0% (30.7–77.9%) in CL-Eu and 149 mg/dl (140–193 mg/dl) and 48.2% (34.9–72.5%) in CL-Hyper, respectively.

### *Conclusions:*

This study suggests that our novel MPC algorithm can safely and effectively control glucose overnight, also when CL control is initiated during hyperglycemia.

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**Abbreviations:** (CGM) continuous glucose monitor, (CL) closed loop, (HbA1c) hemoglobin A1c, (ISF) insulin sensitivity factor, (MAD) mean absolute difference, (MARD) mean absolute relative difference, (MPC) model predictive control, (OL) open loop, (T1DM) type 1 diabetes mellitus, (YSI) Yellow Springs Instruments

**Keywords:** clinical study, closed-loop glucose control, model predictive control, type 1 diabetes mellitus

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## Introduction

Development of a closed-loop (CL) glucose control system, also referred to as an artificial pancreas, has been pursued by type 1 diabetes mellitus (T1DM) researchers for decades.[1] It is expected that a CL system can improve diabetes treatment, i.e., reduce hyperglycemic excursions as well as the risk of hypoglycemia and at the same time improve quality of life in patients with T1DM. The CL system consists of a glucose sensor, an automated control algorithm, and an insulin-delivery device. With advances particularly in glucose sensing technology, the focus on CL glucose control has intensified, and still more study groups are active in this field of research. Each study group has its own strategy for CL control: different glucose sensors and insulin-delivery devices are in use; different mathematical methodologies are applied in the construction of control algorithms; different platforms communicating data between system components have been built; and some groups have extended their system with even further components such as glucagon delivery.[2–18] Impressive work has been conducted by these groups, and landmark results have been achieved, yet there is still a distance to cover before a safe, robust, and fully automated CL system becomes a reality.

In 2008, we founded the DiaCon collaboration with the main objective of developing a CL system. Our reasons for entering the CL research field included a belief that we can contribute to the artificial pancreas scientific community with expertise in modeling and control of stochastic systems that can bring the current state-of-the-art steps forward. We developed an algorithm based on model predictive control (MPC) theory and conducted the first clinical feasibility study in 2011–2012.[18,19] This article presents our approach to CL glucose control, including a description of the clinical setup, details of the control algorithm, and results from the first clinical test of the system. In addition, we discuss differences in CL study protocols and procedures, which pose difficulties with regard to control algorithm performance comparisons.

## Methods

### *Closed-Loop System*

Our system is based on subcutaneous glucose sensing and subcutaneous insulin delivery. Every 5 min, a glucose value is transferred from a Dexcom SEVEN PLUS (Dexcom, San Diego, CA) continuous glucose monitor (CGM) via a USB cable to a laptop computer (HP EliteBook, Hewlett-Packard, Palo Alto, CA). Two programs are running on the laptop: MATLAB (MathWorks, Natick, MA), which is running the control algorithm, and LabVIEW (National Instruments, Austin, TX), which is running a user interface that we developed specifically for CL studies by our group (**Figure 1**). Every 15 min, the CL system gives an insulin dose suggestion. The study physician needs to approve (or overrule) the dose suggestion and manually administer the insulin via the insulin pump (Paradigm Veo, Medtronic, Northridge, CA). Insulin is given as microboluses with 0.025 U increments in addition to a small continuous basal insulin infusion of 0.025 U/h. The latter has been implemented for practical reasons, as the pump cannot administer boluses if the basal rate is shut off.

### *Control Algorithm*

Our controller is an MPC algorithm based on a linear second-order deterministic model and a stochastic model. Details about the controller have been reported elsewhere.[18,19] The deterministic part of the algorithm is specified by three empirically determined patient-specific parameters: insulin sensitivity factor (ISF), insulin action time, and basal insulin infusion rate at the time of CL initiation. Estimation of the stochastic part of the model was based on data from one diabetes patient.[20,21] The controller computes the optimal sequence of insulin administrations based on glucose measurements, previous insulin administrations, predictions from a physiological model describing the glucose–insulin dynamics, and a glucose target level. The glucose target level was set at 108 mg/dl on all study nights. In addition, the maximum allowed bolus size depends on the current glucose level. This safety layer improves the robustness of the control strategy and reduces the risk of hypoglycemia. Before the clinical study, extensive testing of the control algorithm was performed in a simulated T1DM population.[18,19]

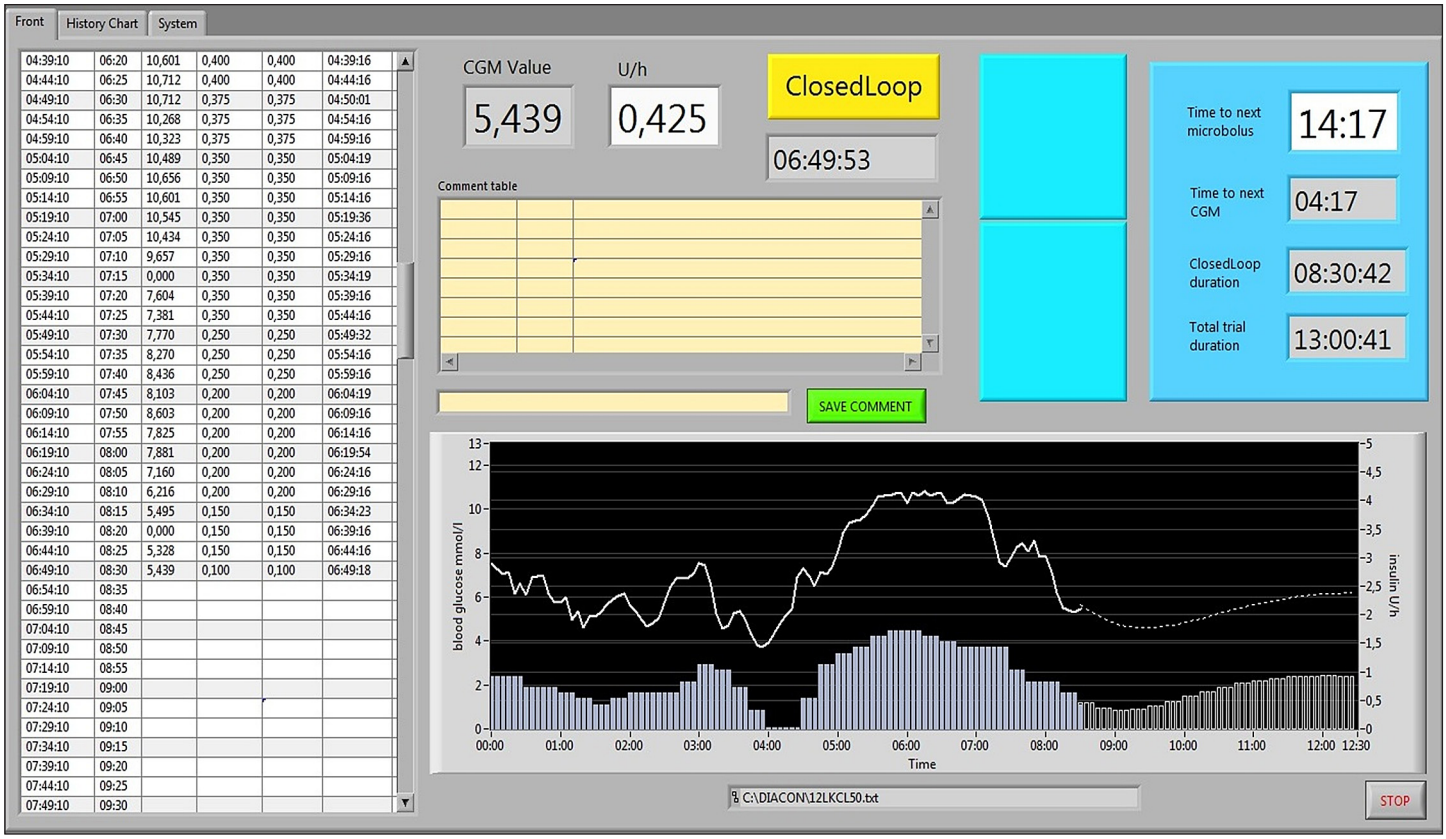


**Figure 1.** User interface developed in LabVIEW for CL glucose control systems. The left panel is a 5 min log for control algorithm insulin proposals and physician insulin administrations. The upper middle panel shows the current CGM value (in mmol/liter) and the most recent insulin dosage (converted to U/h) and below is a log for research team comments. The upper right panel gives time indications. The lower right panel illustrates CGM values (bold curve), CGM predictions (dotted curve), insulin administrations (filled bars), and predicted insulin administrations (empty bars).

### *Study Design*

We conducted two randomized crossover studies. The aim of the first study (study 1) was to compare CL glucose control with conventional open-loop (OL) insulin pump treatment. The aim of the second study (study 2) was to test the performance of the system with blood glucose in the euglycemic (CL-Eu) and hyperglycemic (CL-Hyper) ranges, respectively, at the time of CL initiation. There was no change to the control algorithm between study 1 and study 2. Six patients were recruited for each of the two studies, and each patient had two overnight hospital admissions separated by at least 2 weeks. Both studies were exploratory feasibility studies testing the operability of our study setup and the performance of our control algorithm, with safety as main focus. Reaching statistical significance was not a goal. Primary outcome was number of hypoglycemic events. A hypoglycemic event was defined by one plasma glucose measurement <54 mg/dl. According to protocol, hypoglycemia was immediately treated with intravenous glucose, and if the plasma glucose subsequently dropped below 54 mg/dl, it counted as another hypoglycemic event. Secondary outcomes were time spent in the ranges <70, 70–144, 70–180, >144, and >180 mg/dl; mean blood glucose level; mean insulin concentration; mean insulin infusion rate; and low blood glucose index (a measure of frequency and extent of hypoglycemic episodes).[22]

Eligible patients were aged 18–65 years, were diagnosed with T1DM for more than 2 years, were insulin pump users for more than 1 year, and had a hemoglobin A1c (HbA1c) <8.0%. Pregnant or nursing patients and users of medicine that affected blood glucose (other than insulin) were excluded. The studies were approved by the Regional Ethics Committee (H-4-2011-064) and Danish Medicines Agency (CIV-11-06-000921), and all patients provided written informed consent.

### *Clinical Procedure*

Two CGMs were inserted 2–4 days prior to each study. The one with highest accuracy was connected to the laptop at study start. The other served as a backup. The CGMs were calibrated upon arrival at the hospital and at 21:45 using finger-stick measurements. Prior to the study, the patients calibrated the CGMs as per manufacturer's instruction using their own blood glucose meter, which was also used for calibrations during the study. Patients were instructed not to exercise or consume alcohol in the 24 h preceding the study. On the morning before a study night, patients changed insulin infusion site.

We studied the patients from 17:30–07:00. On arrival at the hospital late in the afternoon, patients were shifted to the study insulin pump, which had the same settings as the patient's own pump. A sampling cannula was inserted in a peripheral vein. At 18:00, an evening meal (white rice, curry sauce, boiled chicken breast, green salad) was served. The size of the meal was determined by patient weight (1 g carbohydrate/kg body weight) and was identical on the two study nights. We used the bolus calculator in the patient's own insulin pump to determine the size of the meal bolus (target 108 mg/dl). In study 2, however, we reduced the meal bolus on CL-Hyper study nights to achieve a hyperglycemic glucose value 4 h after the meal (target 216 mg/dl). No further food or insulin boluses were given.

On OL study nights, the study pump delivered insulin from 17:30–07:00 according to the patient's usual basal rate. On CL study nights, the patient's usual basal rate was administered from 17:30–22:00. This period was intended for control algorithm initialization before closing the loop. At 22:00, we reduced the basal rate to 0.025 U/h, and the controller took over glucose control.

On all study nights, we drew 30 min blood samples for plasma glucose and insulin aspart (NovoRapid, Novo Nordisk, Bagsværd, Denmark) analysis. Plasma glucose was analyzed using the YSI2300 STAT Plus (YSI) from Yellow Springs Instruments, Yellow Springs, OH. If a YSI value was 54–79 mg/dl, an additional sample for plasma glucose determination was taken 15 min later. If a YSI value was <54 mg/dl or if the patient was experiencing prominent symptoms of hypoglycemia, glucose was given intravenously to raise the blood glucose level to 81 mg/dl (calculated using the patient's ISF and insulin-to-carbohydrate ratio). Likewise, intravenous glucose was administered if the plasma glucose value had been in the range of 54–63 mg/dl for two consecutive hours. Patients did not self-administer carbohydrates or correction boluses.

## Results

We included six patients for each of the two studies, but one patient withdrew from study 1 for reasons of discomfort. Characteristics of the five patients (three men) who completed study 1 were age 45 years (43–49 years; median [interquartile range]), body mass index 23.9 kg/m$^2$ (23.7–24.2 kg/m$^2$), HbA1c 7.1% (7.1–7.2%), C-peptide 43 pmol/liter (32–43 pmol/liter; maximum beta-cell stimulation), and total daily insulin dose 0.6 U/kg/day (0.5–0.6 U/kg/day). Characteristics of the six patients (three men) in study 2 were age 31 years (29–39 years), body mass index 25.1 kg/m$^2$ (21.2–26.3 kg/m$^2$), HbA1c 7.4% (6.7–7.4%), C-peptide 45 pmol/liter (33–91 pmol/liter), and total daily insulin dose 0.6 U/kg/day (0.6–0.7 U/kg/day). All patients were treated with insulin aspart.

Hypoglycemic events with plasma glucose <54 mg/dl occurred in two out of the five OL study nights with six and three episodes in each night, respectively. A hypoglycemic event occurred in 2 out of 11 CL study nights (one in study 1 and study 2, respectively), with five events in one night and a single event in the other night. In one CL study night, intravenous glucose was administered because the plasma glucose value had been in the range of 54–63 mg/dl for 2 h. However, the CGM value was never <72 mg/dl. The situations where glucose was administered during CL are depicted in **Figure 2**.

**Table 1** summarizes secondary outcomes of study 1. Glucose values at 22:00 and 22:00–07:00 did not differ on CL and OL study nights. Time in the ranges 70–144 and 70–180 mg/dl favored CL control. Correspondingly, the low blood glucose

index and percentage of time with BG <70 and >144 and 180 mg/dl, respectively, were greater during OL than CL. **Figure 3** illustrates glucose control measured by CGM during study 1.

**Table 2** summarizes secondary outcomes of study 2. As intended, glucose values were significantly different at 22:00 on CL-Eu and CL-Hyper study nights. **Figure 4** illustrates glucose control measured by CGM during study 2.

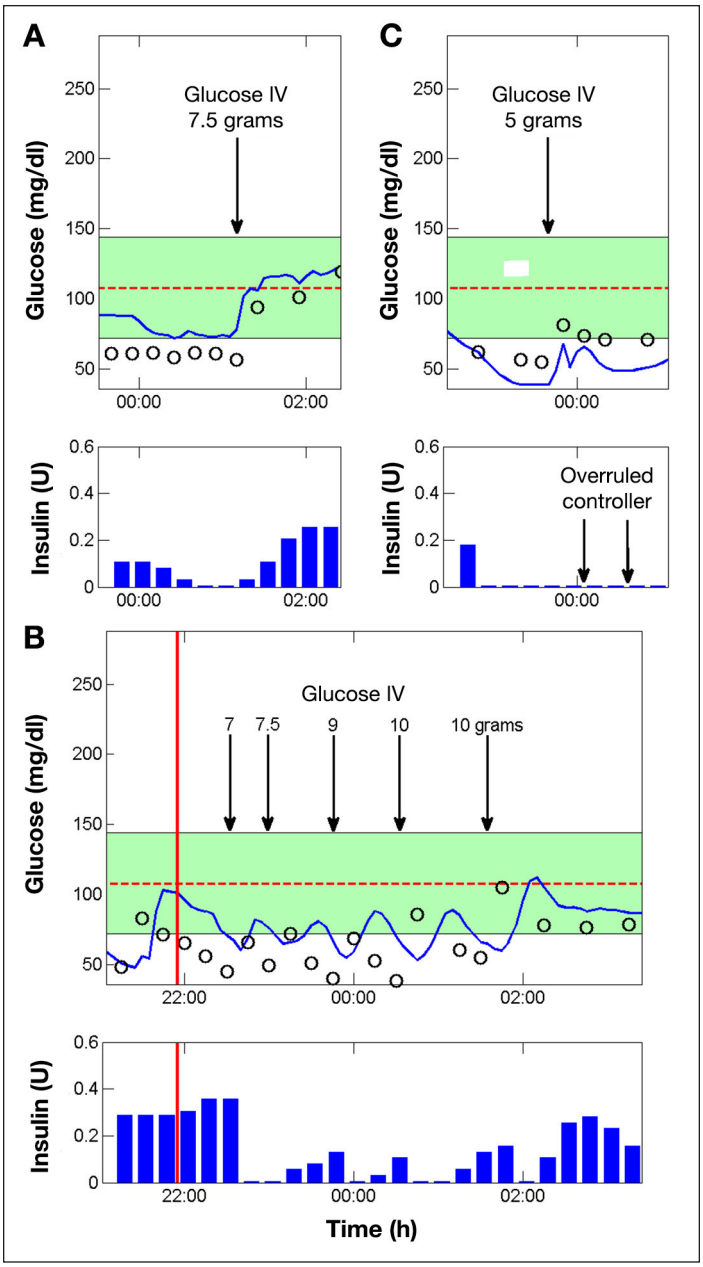


**Figure 2.** Glucose administrations (intravenous) during CL. The target blood glucose was 81 mg/dl and the amount of glucose to be administered was determined by the individual patient's ISF and insulin-to-carbohydrate ratio. **(A)** A situation in which glucose was administered because the plasma glucose value had been in the range of 54–63 mg/dl for 2 h; notice that the sensor value was never below 72 mg/dl. **(B)** Five hypoglycemic events in one CL night. The red line marks CL initiation. **(C)** Hypoglycemic event 2 h after CL initiation. The two overruled controller suggestions were both at 0.025 U/h. IV, intravenous.

On one occasion, the attending physician decided to overrule the insulin suggestion proposed by the controller, and no insulin was administered. The reason for this was a decreasing glucose value despite immediately preceding intravenous glucose administration (**Figure 2C**).

Only once did we deviate from calibration operating procedures and perform an extra CGM calibration.

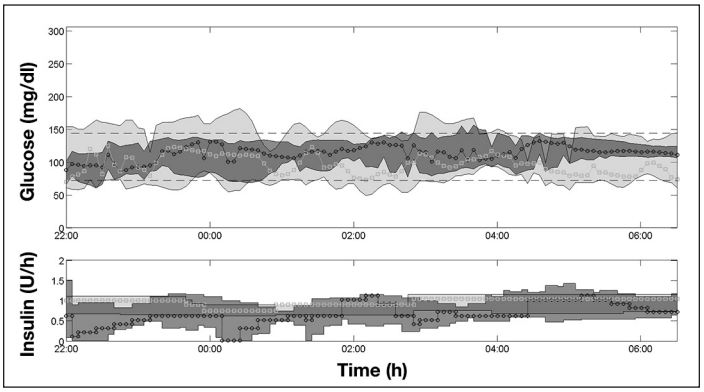


**Figure 3.** Summary of glucose control measured by CGM and insulin delivery during study 1. Light gray curves and areas represent OL study nights. Dark gray curves and areas represent CL study nights. Data are median values with interquartile range. (Upper panel) Glucose measurements. The dotted lines mark the upper and lower limit of the target zone 70–144 mg/dl. (Lower panel) Insulin delivery.

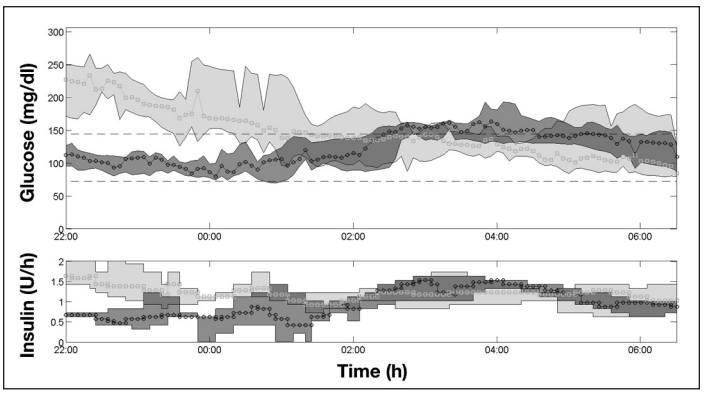


**Figure 4.** Summary of glucose control measured by CGM and insulin delivery during study 2. Light gray curves and areas represent CL study nights with glucose values in the hyperglycemic range at CL start. Dark gray curves and areas represent CL study nights with glucose values in the euglycemic range at CL start. Data are median CGM value with interquartile range. (Upper panel) Glucose measurements. The dotted lines mark the upper and lower limit of the target zone of 70–144 mg/dl. (Lower panel) Insulin delivery.

**Table 1.**
**Summary of Outcomes from Study 1, Secondary Analysis, for the Time Period of 22:00–07:00[a]**

| | OL | | CL | | *P* value | *P* value |
|---|---|---|---|---|---|---|
| | CGM | YSI | CGM | YSI | CGM | YSI |
| Blood glucose at 22:00 (mg/dl) | 70 (60–146) | 104 (70–133) | 95 (85–110) | 72 (65–122) | 0.37 | 0.32 |
| Mean blood glucose (mg/dl) | 90 (74–146) | 83 (70–131) | 108 (101–126) | 108 (92–122) | 0.38 | 0.37 |
| % time spent within 70–144 mg/dl | 67.9 (3.0–73.3) | 26.3 (11.2–84.2) | 80.8 (70.5–89.7) | 67.6 (53.7–85.4) | 0.08 | 0.09 |
| % time spent within 70–180 mg/dl | 67.9 (12.1–90.0) | 26.3 (19.1–84.2) | 90.4 (84.7–99.3) | 89.5 (65.9–100.0) | 0.11 | <0.05 |
| % time spent <70 mg/dl | 13.3 (0.0–48.2) | 5.3 (0.0–34.2) | 9.6 (0.0–15.3) | 10.5 (0.0–34.1) | 0.22 | 0.36 |
| Low blood glucose index | 3.5 (0.1–10.2) | 4.9 (0.3–9.0) | 1.8 (0.8–2.8) | 2.3 (1.1–5.6) | 0.21 | 0.25 |
| Plasma insulin concentration (pmol/liter) | 80.8 (78.4–116.9) | | 71.2 (58.8–119.6) | | 0.13 | |
| Insulin infusion (U/h) | 0.88 (0.75–1.06) | | 0.83 (0.59–0.92) | | 0.23 | |

[a] Data are reported as median (interquartile range). Comparisons were computed using Student's *t*-test.

**Table 2.**
**Summary of Outcomes from Study 2, Secondary Analysis, for the Time Period of 22:00–07:00[a]**

| | CL-Eu | | CL-Hyper | | *P* value | *P* value |
|---|---|---|---|---|---|---|
| | CGM | YSI | CGM | YSI | CGM | YSI |
| Blood glucose at 22:00 (mg/dl) | 113 (94–139) | 124 (117–130) | 232 (184–266) | 248 (223–266) | 0.003 | <0.001 |
| Mean blood glucose (mg/dl) | 121 (117–133) | 133 (126–140) | 149 (140–193) | 157 (133–178) | 0.03 | 0.13 |
| % time spent within 70–144 mg/dl | 69.0 (30.7–77.9) | 53.9 (39.5–73.7) | 48.2 (34.9–72.5) | 52.6 (5.3–63.2) | 0.32 | 0.27 |
| % time spent within 70–180 mg/dl | 100.0 (50.5–100.0) | 77.6 (55.3–100.0) | 75.3 (74.0–85.3) | 65.8 (63.2–73.7) | 0.31 | 0.23 |
| % time spent <70 mg/dl | 0.0 (0.0–30.4) | 0.0 (0.0–7.9) | 0.0 (0.0–10.6) | 0.0 (0.0–0.0) | 0.26 | 0.31 |
| Low blood glucose index | 0.9 (0.7–6.5) | 0.5 (0.0–1.9) | 0.3 (0.0–0.7) | 0.2 (0.0–1.8) | 0.11 | 0.06 |
| Plasma insulin concentration (pmol/liter) | 95.2 (78.6–110.4) | | 116.8 (106.3–124.6) | | <0.001 | |
| Insulin infusion (U/h) | 0.86 (0.75–1.17) | | 1.23 (0.98–1.35) | | 0.02 | |

[a] Data are reported as median (interquartile range). Comparisons were computed using Student's *t*-test.

This was for safety reasons: the reference value was steadily increasing, but the controller had shut off insulin administration because the CGM value had been <54 mg/dl for 40 min. At the time of calibration, the difference between the CGM and the reference value was 126 mg/dl.

Overall mean absolute difference (MAD) between CGM and YSI values was 20 mg/dl (95% confidence interval 0.0–59 mg/dl) and mean absolute relative difference (MARD) was 16.18% (0.0–46.5%). In the time period 22:00–07:00, MAD was 21 mg/dl (0.0–57 mg/dl) and MARD was 19.77% (0.0–56.19%). Of 3564 possible CGM values, 196 (5.5%) were missing.

## Discussion

### *Main Achievements*

This study demonstrates that we have established a functional CL study setup and developed an effective control algorithm for the overnight period. Although this was a feasibility study that was not designed to prove CL superiority, it was affirming to see that time spent in the target range of 70–144 mg/dl increased from a median value of 67.9% during OL to 80.8% during CL control.

### *Strengths and Limitations of the Novel Model Predictive Control Approach*

The key controller challenge in CL glucose control is to compute insulin dosages from uncertain and noisy CGMs, for unannounced meals and exercise, and for large intraindividual and interindividual variability. Our controller is an MPC algorithm that addresses these challenges by handling the stochastic CGM and patient variations using a Kalman filter, by controlling the glucose level to a range rather than a specific glucose value, by providing steady state offset free glucose control, by being robust against patient–model mismatch by its definition of target trajectories and use of low-order models, by being individualized to each patient by use of already available parameters, and by including medical expert rules for safety purposes. The controller includes, combines, and extends key principles from model-based proportional-integral-derivative controllers,[23] previous MPC algorithms,[24–28] fuzzy logic controllers,[29] and novel theoretical MPC insights.[30,31]

Intravenous glucose was administered on three CL study nights (**Figure 2**). In one of the three nights (**Figure 2B**), glucose was actually given five times; however, in the same patient, six glucose administrations were needed on the OL night, indicating that this patient's usual basal rate was too high. As we give patient-specific information, including the 22:00 basal rate to the controller, the too-high basal rate affected controller performance. This demonstrates that, when patient-specific parameters are included in the controller, the patient needs to be fairly well-controlled beforehand and long-term diabetes control needs to be evaluated by CGM and not only HbA1c, which, in this case, was 7.1%.

### *Closed-Loop System Components with Improvement Potential*

Subcutaneous glucose monitoring in CL systems has been rated as the sensing approach with the greatest potential for commercialization in the near future, and it is also the approach adopted by most study groups.[2,3,8,10,29,32] Nevertheless, subcutaneous glucose monitoring remains one of the greatest obstacles to closing the loop. We also encountered CGM challenges. The CL sessions were carried out during hours of only few blood glucose fluctuations (22:00–07:00), and still the MARD was 19.77%. Other studies of this device have reported lower MARDs.[33] For no obvious reason, 5.5% of all possible CGM values were missing. We had prepared our controller for dropouts by implementing a Kalman filter that allows for missing observations. However, we had not prepared for improbable sensor values. In one study, for instance, the patient was hyperglycemic (YSI value 284 mg/dl) in the evening following an underbolused evening meal. The CGM captured this satisfactorily (CGM value 279 mg/dl). Nevertheless, from one value to the next, it made a 270 mg/dl jump, and for 1 h, it gave a glucose value of 9 mg/dl then jumped back to the hyperglycemic "real" range. The controller shut off the insulin in response to the suspected severe hypoglycemic state, which certainly did not improve glucose values. In an OL situation, the patient would intuitively recognize a value of 9 mg/dl as false and ignore it. For the controller to be able to categorize it as false, it needs a strategy for detecting that (1) such a drop in glucose is physiologically impossible and (2) the value in itself is highly unlikely. An outlier detector based on the model parameters' variance could detect inconsistent CGM values. One way of handling the outliers would be to switch off the insulin pump when the CGM values are considered as false and then—if needed—administrate a compensatory bolus when the CGM recovers. However, if the CGM values are false for longer time periods, insulin must be administered to avoid diabetic ketoacidosis. One possibility would be to switch to OL, i.e., to administer the patient's usual basal rate.

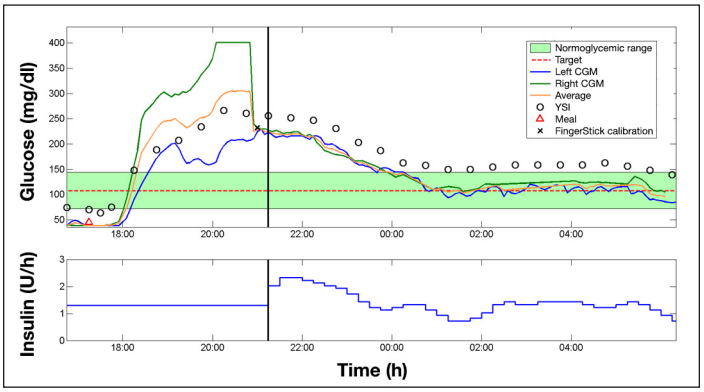


**Figure 5.** Example of CGM system challenges during CL glucose control. The vertical black line marks the initiation of CL control. Notice how the finger-stick calibration at 20:59 aligns the two CGM curves; however, there is a constant offset of approximately 40 mg/dl between CGM and YSI values throughout the night.

**Figure 5** gives an example of CGM challenges met during the study. The curves of the CGM connected to the CL system and the backup CGM are plotted in **Figure 5**. Interestingly, in the interval of 17:30–21:45, the mean of the CGM values was closer to the reference value than either of the two CGMs. Calibrating the CGMs at 21:45 aligned the CGM values but did not bring the mean

closer to the reference (YSI values). This contrasts with previous studies showing that the use of redundant sensors improves CGM accuracy and that the average value of two sensors has substantially lower error than the random sensor value.[34,35] One explanation for this discrepancy could be that we used capillary glucose values for CGM calibration and YSI glucose as reference value, whereas in these previous studies, HemoCue venous glucose values were used both for calibration and reference. It should be mentioned that new and more accurate CGM generations have been launched since the completion of the present study.

### *Study Limitations*

We set up this feasibility study to gain clinical experience with our newly developed control algorithm. Secondly, we used the study to confirm that future extensions of the controller-targeted meal and exercise challenges build on a controller that can handle overnight stabilization of blood glucose. The study situation chosen was simple and did not pose challenges to the controller, such as meals or exercise, which limits the clinical impact of the results. Furthermore, the outcomes of study 1 should be evaluated keeping in mind that patients did not administer correction boluses or have access to carbohydrates that could prevent a pending hypoglycemic episode on OL nights.

### *Performance Comparisons between Closed-Loop Systems*

It is desirable, however problematic, to compare the performance of different CL systems. Three main reasons are the great variations in study protocols (e.g., meals, exercise), differences in study populations, and variable definitions of outcome parameters, such as target ranges and hypoglycemia. However, system performance and thus study outcomes are also affected by other less obvious factors not directly related to the CL system itself. One example is CGM calibration procedures. Frequency and method of calibration both affect study outcomes. In a number of CL studies—including our own—capillary glucose was used for calibration as per manufacturers' instruction whereas others used the reference glucose value (YSI or HemoCue) for calibration.[10,36,37] In addition, some study protocols prescribed CGM calibrations in response to sensor drift.[2,8,13,38] Use of reference glucose values and drift-triggered calibrations will invariably keep the CGM value closer to the reference, thereby improving CGM accuracy but also overall study outcomes. Another example of procedures that affect study outcomes is hypoglycemia management. Few studies practice identical procedures for hypoglycemia management. Time spent in hypoglycemia is dependent on the controller target setting, the threshold for administering hypoglycemia treatment, the amount of carbohydrate administered in case of a hypoglycemic episode, and also the circumstance that in some studies carbohydrates are administered already when hypoglycemia is predicted. A third example is patient instructions for OL study nights, e.g., whether patients are allowed to give correction insulin boluses and adjust the basal rate, whether they have access to carbohydrates, and whether they are informed about reference glucose values and trends.

## Conclusions

We have presented the DiaCon approach to CL glucose control and reported results and experiences from the first clinical study of our CL system. One of the greatest challenges met was irregularities in CGM input, and CGM inaccuracy was the direct cause of a hypoglycemic event. To improve system robustness, further improvements in sensor technologies are needed. In addition, we observed that a stochastic model identified from patient data, a robust controller, and adequately determined patient-specific parameters were important attributes for good and safe CL glucose MPC control.

Currently, various aspects of CL glucose control are being explored in various study settings and study populations. Performance comparisons between the different CL systems are difficult for a number of reasons, as pointed out earlier. We suggest that, if direct comparisons between the results of CL studies should be made possible, international protocol guidelines are needed.

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**Disclosures:**

Kirsten Nørgaard has received speaker honorariums from Roche Diagnostics, Animas, and Medtronic and serves on the advisory board of Medtronic.

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