Background and Aims: As evidence emerges that artificial pancreas systems may improve clinical outcomes for patients with type 1 diabetes, the burden of this disease will hopefully begin to be alleviated for many patients and caregivers. However, a decrease in burden potentially means patients will be slower to act when devices stop functioning appropriately. One particular device failure involves a loss in infusion set actuation (LISA), where the apparent injected insulin fails to affect the patient's glucose as expected. Alerting patients to these events in real-time has the potential to reduce hyperglycemia following a LISA.

Methods: A LISA detection algorithm was implemented in a randomized cross-over study with closed-loop and sensor-augmented-pump arms on 19 subjects. Each arm lasted two weeks. Participants wore infusion sets for up to 7 days to provoke failures. A clinician contacted patients to confirm and repair LISAs detected by the algorithm. LISAs were determined by (i) failed correction doses, (ii) ketones >0.6, (iii) insulin leaking at insertion sites, and (iv) pump-occlusion alarms.

Results: The LISA detection algorithm achieved a sensitivity of 85% (n = 27) while issuing only 0.22 false positives per day. Furthermore, the artificial pancreas using zone model predictive control with LISA detection limited the mean hyperglycemia exposure (> 250 mg/dL) in the four hours preceding a LISA to 46.4 minutes, compared to 103.0 minutes during sensor-augmented-pump therapy (p-value 0.01).

Conclusions: As patient burden is reduced by each generation of advanced diabetes technology, fault detection algorithms will help ensure that patients are alerted when they need to manually intervene.

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OPEN TO CLOSED-LOOP TRANSITION SCHEMES FOR IN VIVO GLUCOSE CONTROL

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Background and Aims: Continuous Subcutaneous Insulin Infusion (CSII) treatments for people with type 1 diabetes can combine the use of a smart insulin pump with a Continuous Glucose Monitor (CGM) and a control algorithm to improve the regulation of the insulin delivery. New control algorithms need to be tested in clinical trials under strictly safety conditions for the patients.

Methods: In this work, a safety layer called the SAFE loop (Revert et al., IEEE-TBME 2013) is reformulated to be employed during clinical trials in two different ways: the Time Enable mode, which gives a criterion for the transition between open and closed-loop therapy in hybrid configurations, and the Amplitude Enable mode, which diminishes the risk of an hypoglycemic event when testing fully closed-loop algorithms by delimiting the Insulin-On-Board (IOB) profile of the new control algorithm with the IOB profile corresponding to the usual open-loop therapy of the patient (or a factor of it).

Results: In-silico trials show how using the Time Enable method the transition from open (bolus) to closed-loop is made automatically and gradually, resulting in a bumpless mechanism which improves the controller response. In the case of the Amplitude Enable mode, the results show how the patient is protected from hypoglycemia even when controller gain is disproportionally large, as shown in the figure below.

Conclusions: Two IOB constraint profiles are proposed for its use in clinical trials, giving rise to a safe mechanism for in vivo testing both hybrid and fully closed-loop controllers.

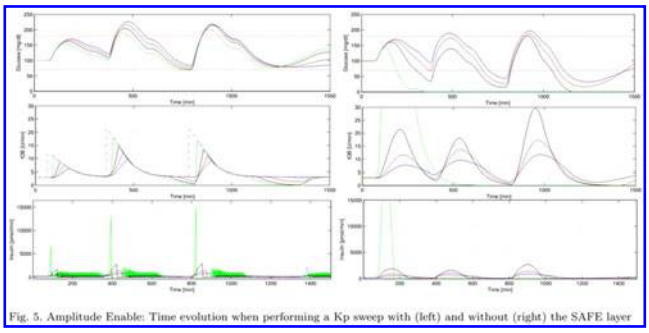

Fig. 5. Amplitude Enable: Time evolution when performing a Kp sweep with (left) and without (right) the SAFE layer

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CORRELATING THE ESTIMATED INSULIN ACTION PEAK EFFECT WITH PATIENT CHARACTERISTICS IN THE 670G PIVOTAL TRIAL

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Background and Aims: The data set from the pivotal trial for the Medtronic MiniMed 670G hybrid closed loop system was used to estimate the insulin action peak effect (Teff) for individual subjects using a mathematical model. Teff was then correlated with a variety of patient variables and measures of glycemia.

Methods: Teff was determined in 61 subjects (out of the 124 pivotal trial participants) to be 211 ± 30 minutes (median ± STD). In the Table, the Pearson's correlation-coefficient (R) between Teff and the subjects' characteristics is given.

Results: The results show a strong positive correlation between Teff and A1C after 3 months of the use of the 670G hybrid closed loop system. There was essentially no correlation between Teff and age, duration of diabetes, or total daily dose of (TDD) after 3 months of 670G use.

Table. Correlation coefficient (R) between Teff and A1C, Diabetes Duration, Total Daily Dose of Insulin and Age

Measurement	R
A1C measurement after 3 months of using the 670G	0.40
Duration of diabetes	–0.17
TDD after 3 months of 670G use	–0.10
Age	0.07

Conclusions: These data suggest that the speed of insulin action is an indicator of the effectiveness of intensive insulin therapy. Since the direction of the relationship is not known, it is also possible that glucose toxicity can increase Teff. However, Teff is likely one of many factors that accounts for insulin therapy effectiveness.