Real-time basal insulin attenuation based on continuous glucose monitoring (CGM): assessment of state-of-art algorithms in 14-day in silico scenario

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1. INTRODUCTION

Automatic attenuation of insulin pump basal delivery is employed as a safety measure against hypoglycemia in open- and closed-loop type 1 diabetes (T1D) therapies. Three popular algorithms proposed in the literature are: brakes (B) and power brakes (PB), based on hypoglycemia risk index calculated from original and predicted CGM data, respectively [1], and PB with insulin on board (IOB-PB) [2]. B and PB were tested on short scenarios in absence of meals. IOB-PB was assessed on a single-day scenario.

2. AIM

The aim is to compare B, PB and IOB-PB algorithms on a 14-day in silico scenario by using a recently developed model of T1D patient decision-making (T1D-DM) [3] in which an ad hoc basal insulin attenuation module is implemented.

3. ALGORITHMS

Brakes (B) [1]:

Risk index:

$$R(G(t)) = \gamma \cdot \left[(ln(G(t)))^{\alpha} - \beta\right]^2$$

Attenuation factor:

$$\Phi_{att}(R(G(t))) = \frac{1}{1 + \Gamma \cdot R(G(t))}$$

Basal insulin attenuation:

$$J_{basal}^{mod}(t) = \Phi_{att}(R(G(t))) \cdot J_{basal}(t)$$

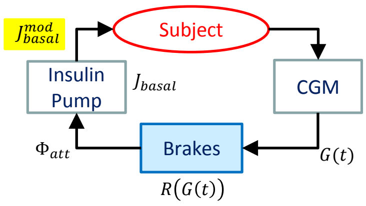

Fig. 1. Scheme of the B algorithm.

Power Brakes (PB) [1]:

Prediction by Kalman filter:

$G(t) \rightarrow \hat{G}(t)$

Risk index: $R(\hat{G}(t))$

Attenuation factor:

$\Phi_{att}(R(\hat{G}(t)))$

Basal insulin attenuation:

$$J_{basal}^{mod}(t) = \Phi_{att}(R(\hat{G}(t))) \cdot J_{basal}(t)$$

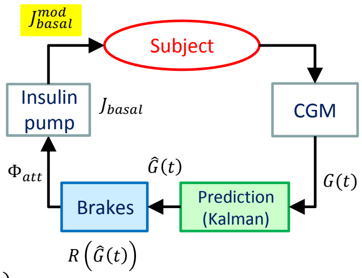

Fig. 2. Scheme of the PB algorithm.

Power Brakes with IOB (IOB-PB) [2]:

Linear prediction: $G(t) \rightarrow \hat{G}(t)$

Calculation of IOB: $I_c(t)$

Prediction corrected for IOB:

$\breve{G}(t) = \hat{G}(t) - 0.5(I_c(t) \cdot CF)$

CF=correction factor

Risk index: $R(\breve{G}(t))$

Attenuation factor: $\Phi_{att}(R(\breve{G}(t)))$

Basal insulin attenuation:

$$J_{basal}^{mod}(t) = \Phi_{att}(R(\breve{G}(t))) \cdot J_{basal}(t)$$

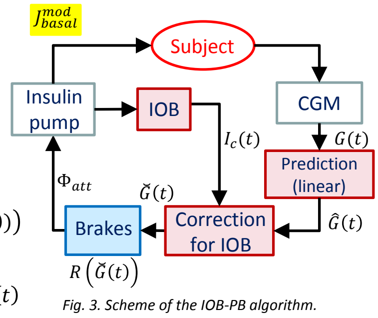

Fig. 3. Scheme of the IOB-PB algorithm.

4. THE SIMULATION FRAMEWORK

A module implementing the algorithms for basal insulin attenuation (E) was incorporated in the T1D-DM model of [3], which simulates the blood glucose (BG) profiles of T1D virtual subjects making treatment decisions based on glucose monitoring devices.

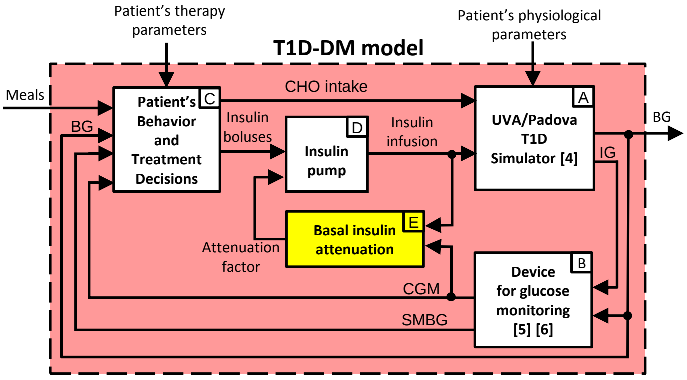

Fig. 4. Schematic representation of the T1D-DM model with the basal insulin attenuation module.

4. THE BASAL INSULIN ATTENUATION MODULE

The basal insulin attenuation module implements the B, PB and IOB-PB algorithms and is structured as follows:

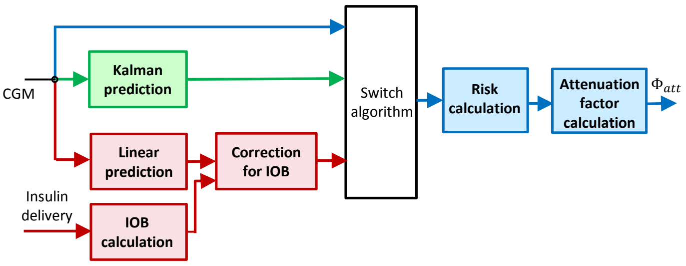

Fig. 5. Schematic representation of the basal insulin attenuation module.

5. IN SILICO TRIAL AND METRICS

100 adult virtual subjects, 2 weeks (3 meals per day), 4 basal insulin scenarios: no basal insulin modulation (no mod) and basal insulin attenuation by B, PB and IOB-PB. In all the scenarios, insulin boluses and hypotreatments are given according to SMBG measurements.

Metrics used for assessment are time in 70-180 mg/dl [h/day], time below 70 mg/dl [min/day] and time above 180 mg/dl [h/day].

5. RESULTS

Comparison of the algorithms in a representative virtual subject:

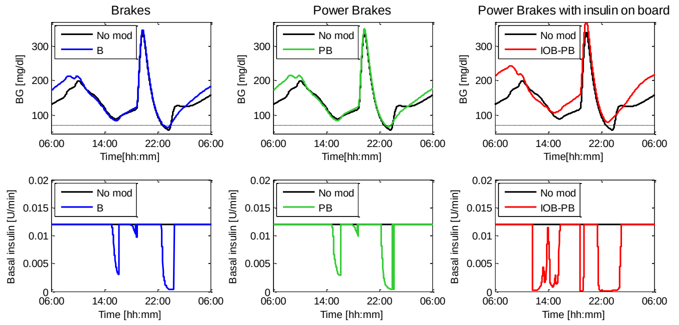

Fig. 6. B, PB and IOB-PB vs no mod in a representative virtual subject.

IOB-PB allows prevention of the nocturnal hypo event at time 23:00 (right panels). B and PB cannot avoid the event, but are, however, able to reduce its duration (left and middle panels).

Table 1: Median and interquartile range (in brackets) of the metrics for the four simulated scenarios

Scenario	Time below 70 mg/dl [min/day]	Time in 70-180 mg/dl [h/day]	Time above 180 mg/dl [h/day]
No mod	26.9 [12.4 - 63.4]	15.0 [12.6 - 17.5]	8.5 [5.8 - 10.9]
B	24.4 [10.1 - 51.5]	14.5 [11.9 - 17.2]	9.0 [6.4 - 11.3]
PB	23.1 [9.0 - 49.3]	14.5 [12.2 - 17.3]	9.0 [6.3 - 11.3]
IOB-PB	9.0 [0.0 - 29.0]	13.3 [10.7 - 15.8]	10.4 [7.9 - 13.0]

Compared to the no modulation scenario:

- B and PB slightly reduce time below 70 mg/dl but increase of 0.5 h/day the median time above 180 mg/dl;
- IOB-PB drastically reduces time below 70 mg/dl but increases of about 2 h/day the time above 180 mg/dl.

6. CONCLUSIONS

Literature algorithms for real-time attenuation of basal insulin based on CGM were implemented in a novel simulation framework (relying on the UVA/Padova T1D simulator) usable to perform multiple-day in silico clinical trials. B, PB and IOB-PB algorithms, in particular, were compared in a two-week trial. The IOB-PB showed the best performance in reducing hypoglycemia, albeit increasing hyperglycemia of almost 2 h/day.

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