SMART INSULIN DOSING FROM THE REAL-TIME ASSESSMENT OF INSULIN EFFECTIVENESS IN TYPE I DIABETES

Chiara Fabris and Marc Breton

Center for Diabetes Technology, University of Virginia, Charlottesville, VA, USA

Introduction & aim

Imperfect insulin replacement is a cause of hypo/hyperglycemia and increased BG variability in T1D. Insulin sensitivity (SI) is a primary factor mediating BG responses to administered insulin.

AIM: To develop a method for **optimal insulin dosing** in T1D leveraging the real-time estimation of Insulin Effectiveness (IE), an index related to SI, from CGM and pump data.

Methods

IE ESTIMATION FROM KALMAN FILTER

- MEAL MODEL: feed-forward model to describe meal absorption and estimate CHO rate of appearance into plasma
- INSULIN MODEL: feed-forward model to describe s.c. insulin transport and estimate plasma insulin concentration
- CORE LOG-MODEL: 3-states model embedded in the KF which describes glucose-insulin dynamics in a logarithmic risk-space and provides estimates of CGM, insulin action (X), and IE

MEAL MODEL

$$\begin{cases} \dot{Q}_0 = -k_1(Q_0 - M) \\ \dot{Q}_1 = -k_2(Q_1 - Q_0) \\ \dot{Q}_2 = -k_3(Q_2 - Q_1) \\ R_a = Q_2/(Q_2 + \gamma) \end{cases}$$

INSULIN MODEL

$$\begin{cases} \dot{I}_1 = -k_d I_1 + J \\ \dot{I}_2 = -k_d I_2 + k_d I_1 \\ \dot{I}_p = -k_{cl} I_p + k_d I_2 \end{cases}$$

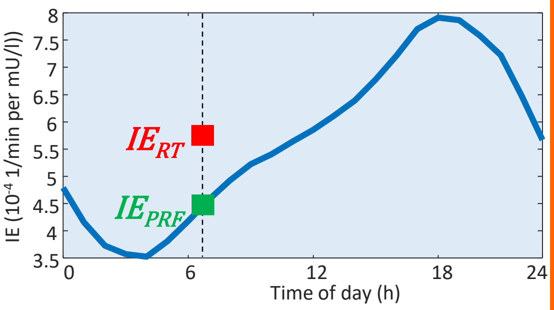
LOG MODEL

$$\begin{cases} \log(\dot{G}/G_b) = -p_1 \log(G/G_b) - p_2 \log(X/X_b) + p_3 R_a \\ \log(\dot{X}/X_b) = -p_4 \log(X/X_b) + p_4 I_p/(V_I\, BW) \\ \log(\dot{IE}/IE_b) = -p_5 \log(IE/IE_b) \end{cases}$$

IE PROFILING ALGORITHM

A **patient-specific IE profile** is drawn by applying the KF onto CGM, meal, and insulin data collected over 30d of monitoring in the field. The 24h IE profile is obtained by:

1. estimating IE hourly across the entire data collection period
2. averaging IE estimates obtained from all days at the same time
3. smoothing the obtained 24h profile (6h moving average filter)



IE-INFORMED SMART BOLUS

At the time of meals, IE is estimated using the KF; the **smart bolus** is then computed as a standard bolus modulated by the ratio of usual (from the IE profile) and real-time IE estimates, while systematic circadian fluctuations are managed by retrospective tuning of therapy parameters (CR/CF profiles).

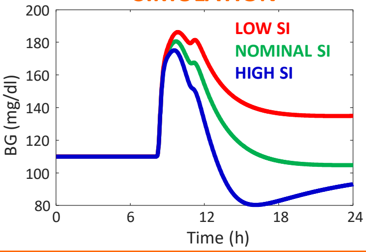
$$B_{IE} = \frac{IE_{PRF}}{IE_{RT}}\left(\frac{CHO}{CR} + \frac{CGM - TGT}{CF} + IOB_{BSL}\right) - IOB_{TOT}$$

SMART BOLUS ALGORITHM VALIDATION

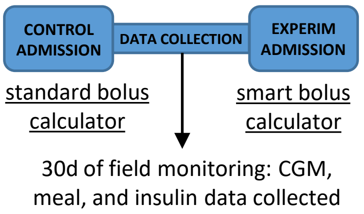
The smart bolus advisor was tested in:

- SIMULATION: UVa/Padova T1D simulator, 100 virtual subjects, 1-meal scenario with varying SI
- CLINICAL TRIAL: NCT02558491, 5 subjects, 2 admissions of 2 days each, standard (control) vs smart (experimental) bolus calculator

SIMULATION



CLINICAL TRIAL

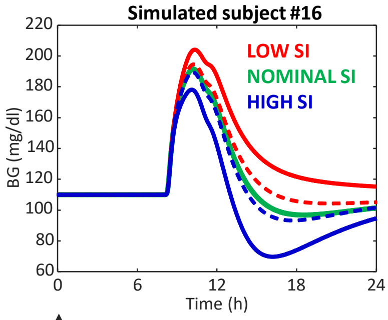


Results

RESULTS FROM SIMULATED DATA

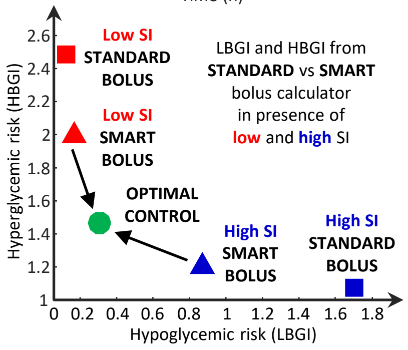
Example of the smart bolus effect (---) on meal regimen as compared to standard therapy (–) and optimal control (–):

- **low SI scenario**: decreased postprandial peak and BG AUC
- **high SI scenario**: avoided postprandial hypoglycemia



Results from risk space analysis (**LBGI/HBGI**) with smart bolus and standard bolus calculator, as compared to optimal control:

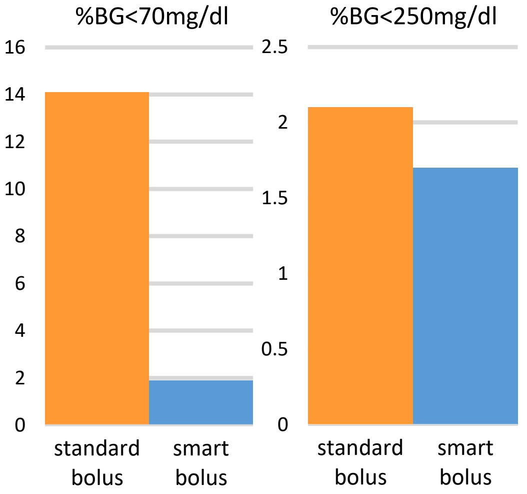
- **low SI scenario**: reduced HBGI
- **high SI scenario**: reduced LBGI
- smart bolus control tends towards optimal control



PRELIMINARY RESULTS FROM REAL DATA

As compared to standard therapy, the smart bolus allowed to decrease postprandial:

- percent BG<70mg/dl from 14.1% to 1.9%
- percent BG>250mg/dl from 2.1% to 1.7%



Conclusions

We propose a new, data-oriented paradigm to optimize insulin dosing in T1D from the real-time assessment of the patient's current insulin need from sensor and pump data.

Address for correspondence: **cf9qe@virginia.edu**