Dermal Glucose Sensing Can Improve Time In Range and Minimize Severe Hypoglycemia

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Introduction: Time in Range (TIR) is a critical metric of glycemic control. Currently available CGMs sensing in the subcutaneous tissue provide close to real-time glucose monitoring, but have a major limitation related to accuracy and long time lag (10-15 minutes), which could delay the management of glucose fluctuations and lead to recurrent and/or severe hyper or hypoglycemia. This subsequently reduces TIR and results in higher HbA1C levels.

Methods: Subjects with Type 1 DM (n=55) were enrolled in a clinical study at two US-based clinical centers and wore the novel dermal CGM, plus Abbott Libre 3 or Dexcom G7, all were compared to a YSI-glucose analyzer. Time lag data was analyzed using the two-compartment model. We used the in-silico PID controller model with 30 simulated subjects (adults and adolescents) to evaluate the consequences of long time lags and predict outcomes associated with a shorter time lag, related to hypoglycemia and time in range. The in-silico PID controller is similar to the Medtronic controller described in literature.

Objectives: To evaluate the performance of a dermal CGM developed by Laxmi Therapeutic Devices in sensing glucose with a shorter time lag, and the impact of this shorter time lag on improving TIR and reducing the frequency and severity of hypoglycemia.

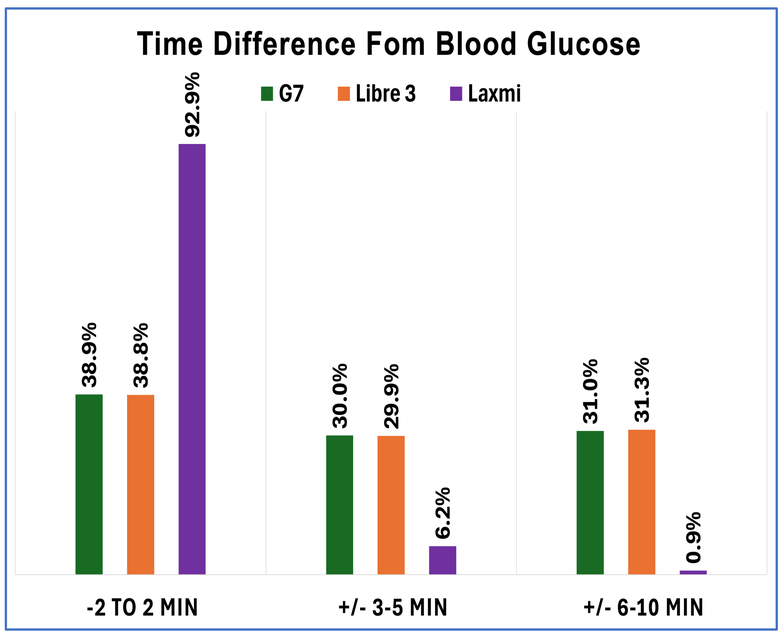

Figure 1: Time Difference From Blood Glucose

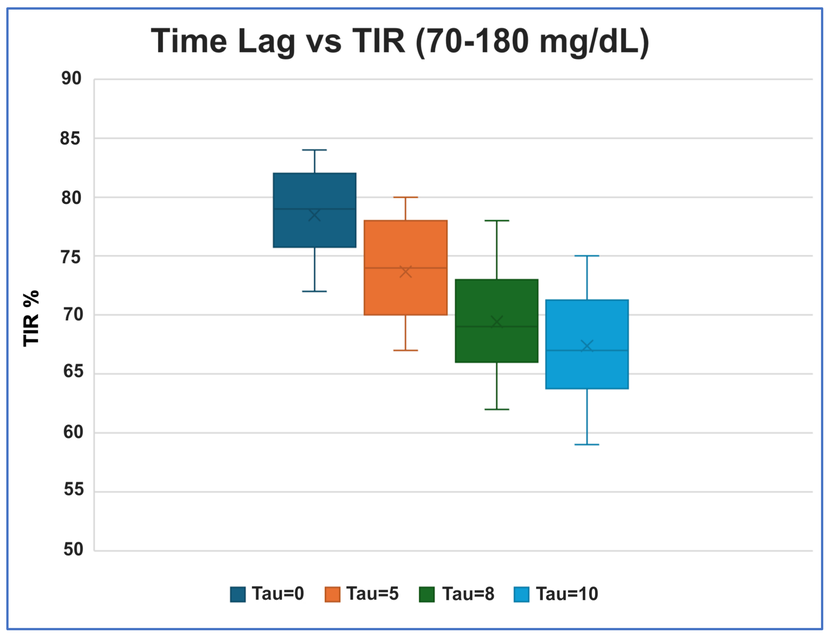

Figure 2: Time Lag vs. TIR

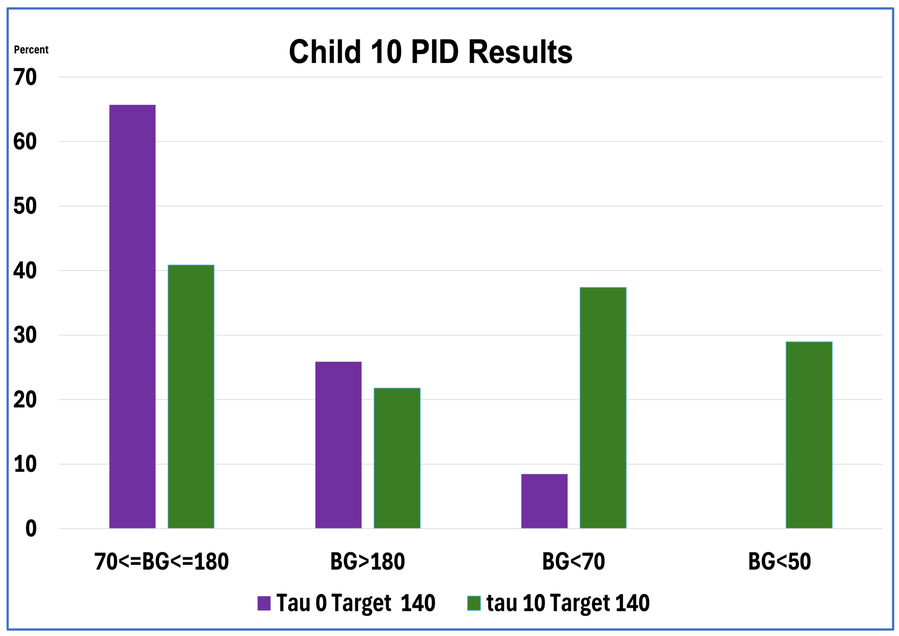

Figure 3: Impact of CGM Time Lag on TIR Distribution at 140 mg/dL Glucose Target: 0 Minimizes Severe Hypoglycemia

Results: The vast majority (92.9%) of the dermal sensors had minimal time difference from blood glucose (time lag, tau) that ranged between 0-2 mins, while commercial CGMs had a varying distribution of tau, up to +/-10 minutes **(Figure 1)**.
We used the PID controller to evaluate the consequences of this difference in time lag. Using the controller, the PID coefficients were manually optimized for TIR for each patient. In general, for an optimized adult subject, target glucose range 70-180 mg/dL, TIR was reduced from 86% to 71% by increasing time lag from 0 to 8 minutes. For adolescent subjects, TIR was reduced from 73% to 65% by implementing an 8-minute time lag. **Figure 2** shows the continuous relationship between Time lag and TIR.
We also evaluated the effect of short tau on the ability to minimize severe hypoglycemia. **Figure 3** summarizes the PID control (Medical Device Technology) simulations for Child 10 using optimized parameters. Two scenarios were tested: target glucose 140 mg/dL with tau=0 and target 140 mg/dL with tau=10 minutes. The PID controller was optimized individually for tau=0 and tau=10 CGM signals.
With a glucose target of 140 mg/dL and no time lag, no BG < 50 mg/dL was observed with tau=0, whereas tau=10 led to ~30% BG < 50 mg/dL. Moreover, tau=0 resulted in ~40% less hypoglycemia (< 70 mg/dL) compared with tau=10 minutes. In the typically desired glucose range of 70-180 mg/dL, tau=0 resulted in a higher percentage of time in this range. Moving frm tau=0 to tau=10 reduced time in the BG > 180 mg/dL range, but at the cost of substantially more hypoglycemia (<70 and <50 mg/dL). The increase in hypoglycemia is explained by insulin over administration, observed with tau=10 **(Figure 4)**, which is nearly double that administered with tau=0.

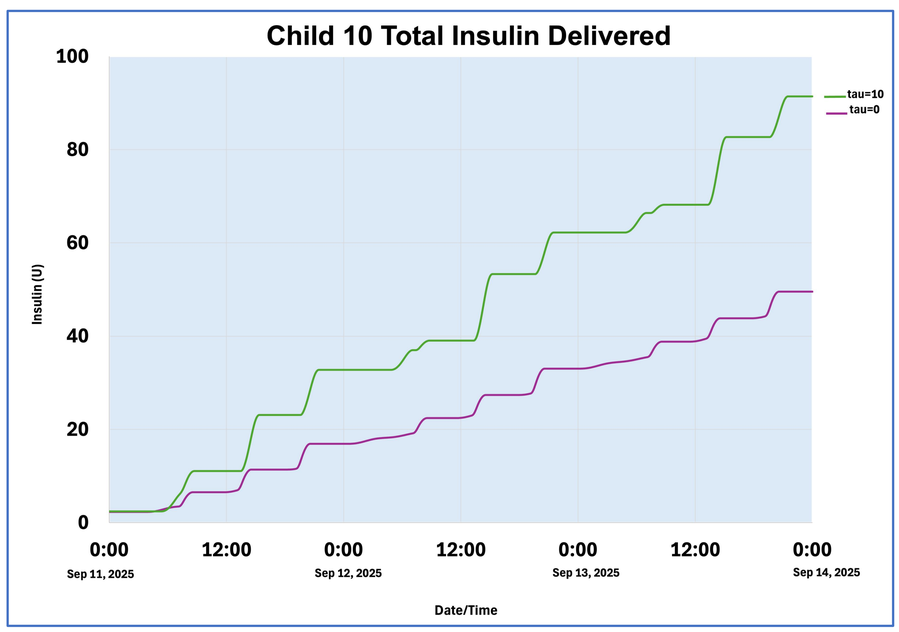

Figure 4: Impact of CGM Time Lag on PID-Driven Insulin Administration

Conclusion: The reduction in tau with dermal sensing compared to commercial CGMs, by a factor of 5-10, suggests that the "Look Forward Algorithms" of existing CGM providers do not match blood glucose as precisely as dermal sensing. The in-silico PID controller data demonstrates that with tau=10, severe hypoglycemia is a major problem, whereas shorter tau is associated with improvement in TIR, and reduction in the overall frequency and severity of hypoglycemia. This highlights the clinical relevance of CGM's tau in guiding insulin delivery. Clinicians will soon have the opportunity to increase TIR by using a dermal CGM that more closely reflects blood glucose levels in closed loop therapy, which can lead to greater patient confidence, adherence, and a better quality of life for individuals with diabetes.

Takeaway: Faster and closer alignment of dermal CGM readings with blood glucose can improve TIR and enable more precise insulin therapy.