

BACKGROUND

Currently available CGMs sensing in the deep subcutaneous tissue provide close to real-time glucose monitoring, but have a major limitation related to accuracy and longer time lag (10-15 minutes), which could delay the management of glucose and lead to recurrent and/or severe hyper or hypoglycemia, especially during rapidly changing glucose levels, resulting in a lower TIR and a higher HbA1C levels.

OBJECTIVES

To evaluate the performance of a dermal sensor developed by Laxmi Therapeutic Devices in sensing glucose with a shorter time lag (t) and better accuracy, especially at high glucose rates of change and during hypoglycemia, and the overall impact of a shorter time lag on the TIR.

METHODS

We evaluated 55 subjects with type-1 DM enrolled at two US-based clinical sites. Subjects wore Laxmi CGM that was compared to frequent YSI plasma blood samples over three in-clinic sessions spanning 7 days. Simultaneously, subjects wore one of two commercial CGMs: Abbott Libre 3 or Dexcom G7.

Data was analyzed using the two-compartment model (Figure 1). In this model, the constant K_{21} is for glucose arrival from blood to ISF, while K_{02} is for glucose leaving the ISF to the local tissue. Panel B shows the response of ISF glucose to a step change in blood glucose and defines τ , the 2-compartment time constant.

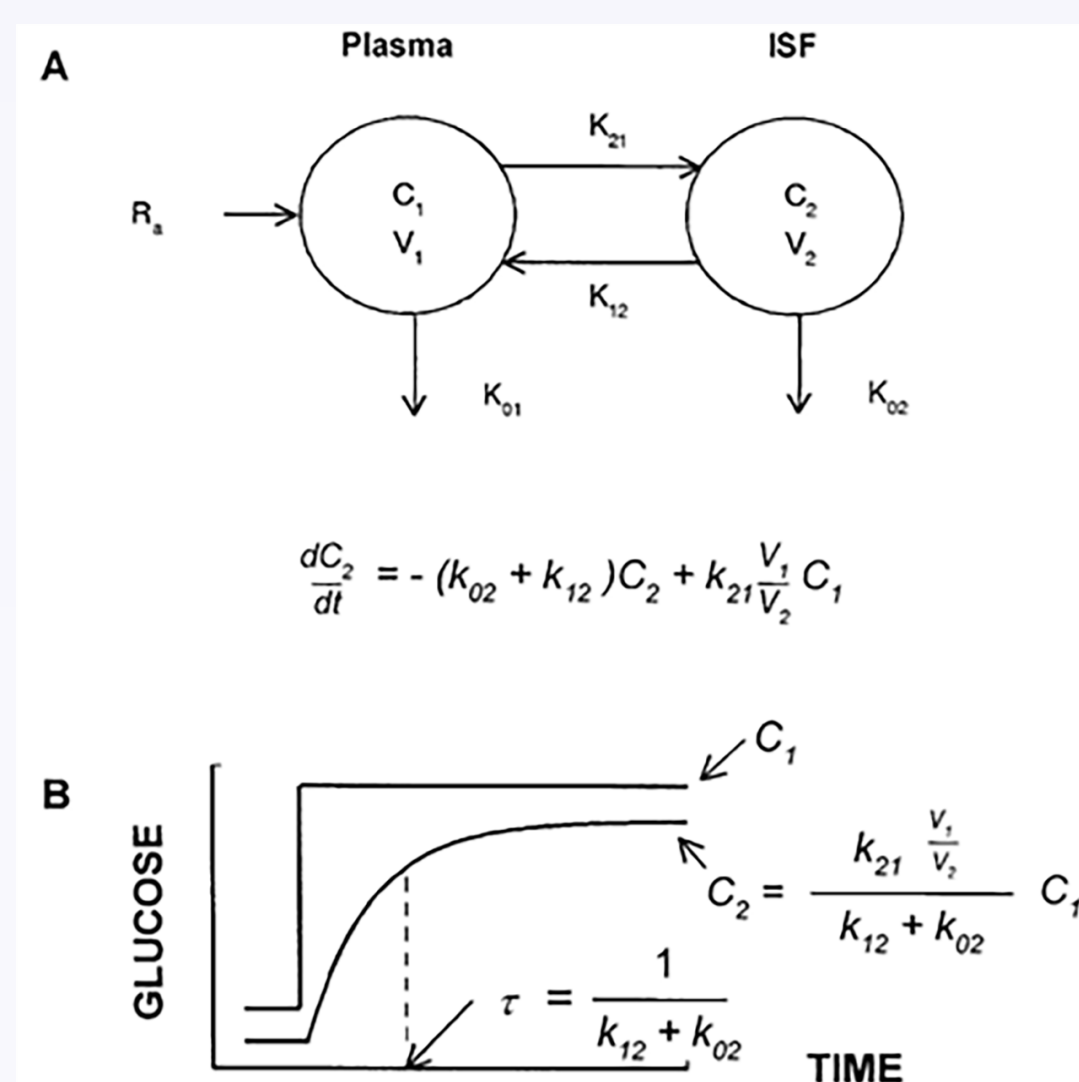


Figure 1: The Two-Compartment Model

RESULTS

Data from 55 subjects demonstrated fast kinetics as most of the Laxmi dermal sensors (> 92.9%) had time lag (t) that ranged between 0-2 mins (Figure 2).

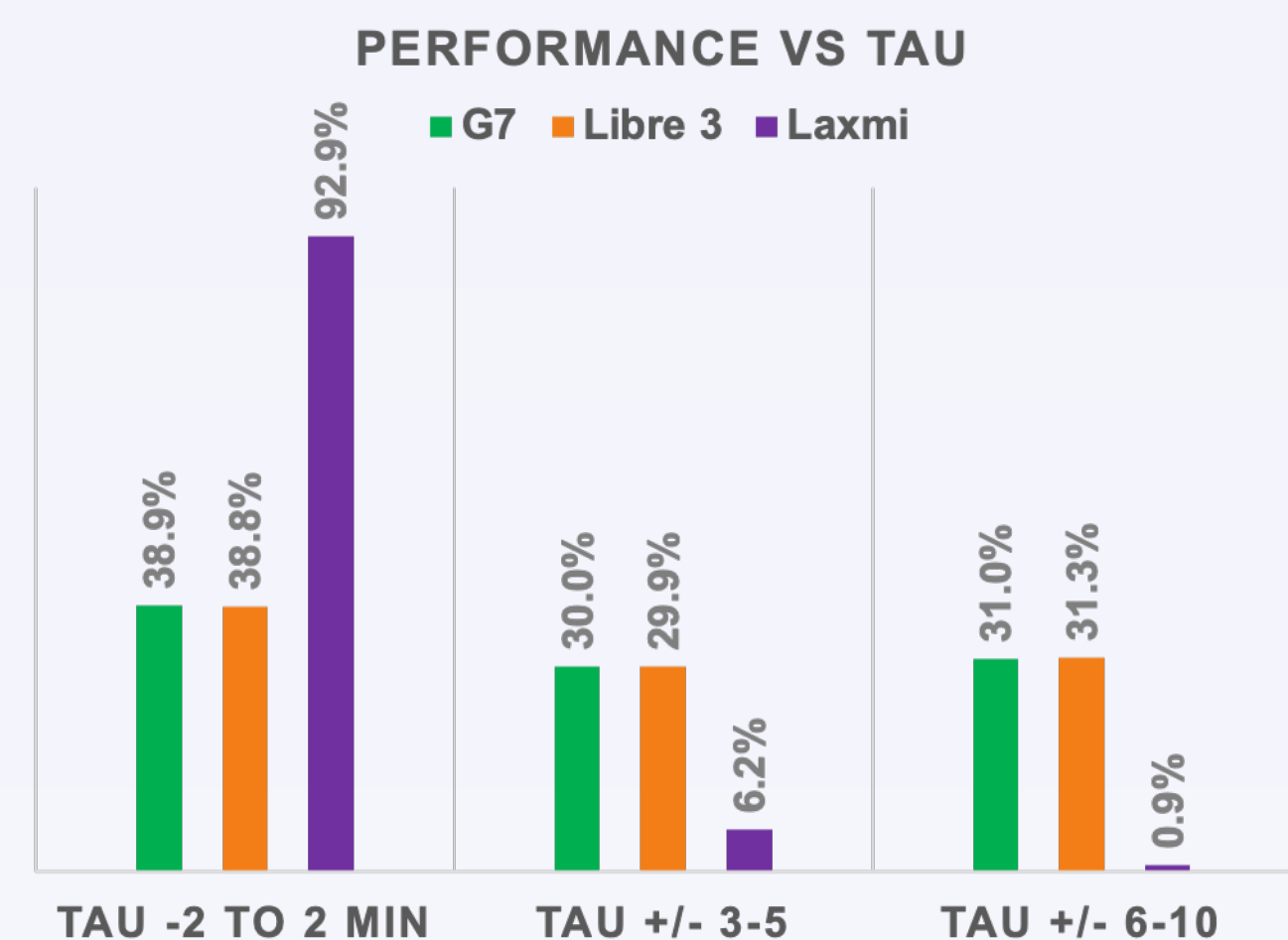


Figure 2: Percentage of Sensors Within Tau Ranges, by CGM Type

Commercial CGMs had a varying tau distribution, of up to 10 minutes. This reduction in t with dermal sensing compared to commercial CGMs by a factor of 5-10 suggests that the "Look Forward Algorithms" of existing CGM providers were not as effective as dermal sensing in this trial. We investigated the success of this algorithm and compared it to dermal sensing. Figure 3 shows a real-world example of a CGM that overestimated a subject's glucose levels, which led the subject to overdose on Insulin, ultimately resulting in severe hypoglycemia (two values of 39 mg/dl, documented by YSI).

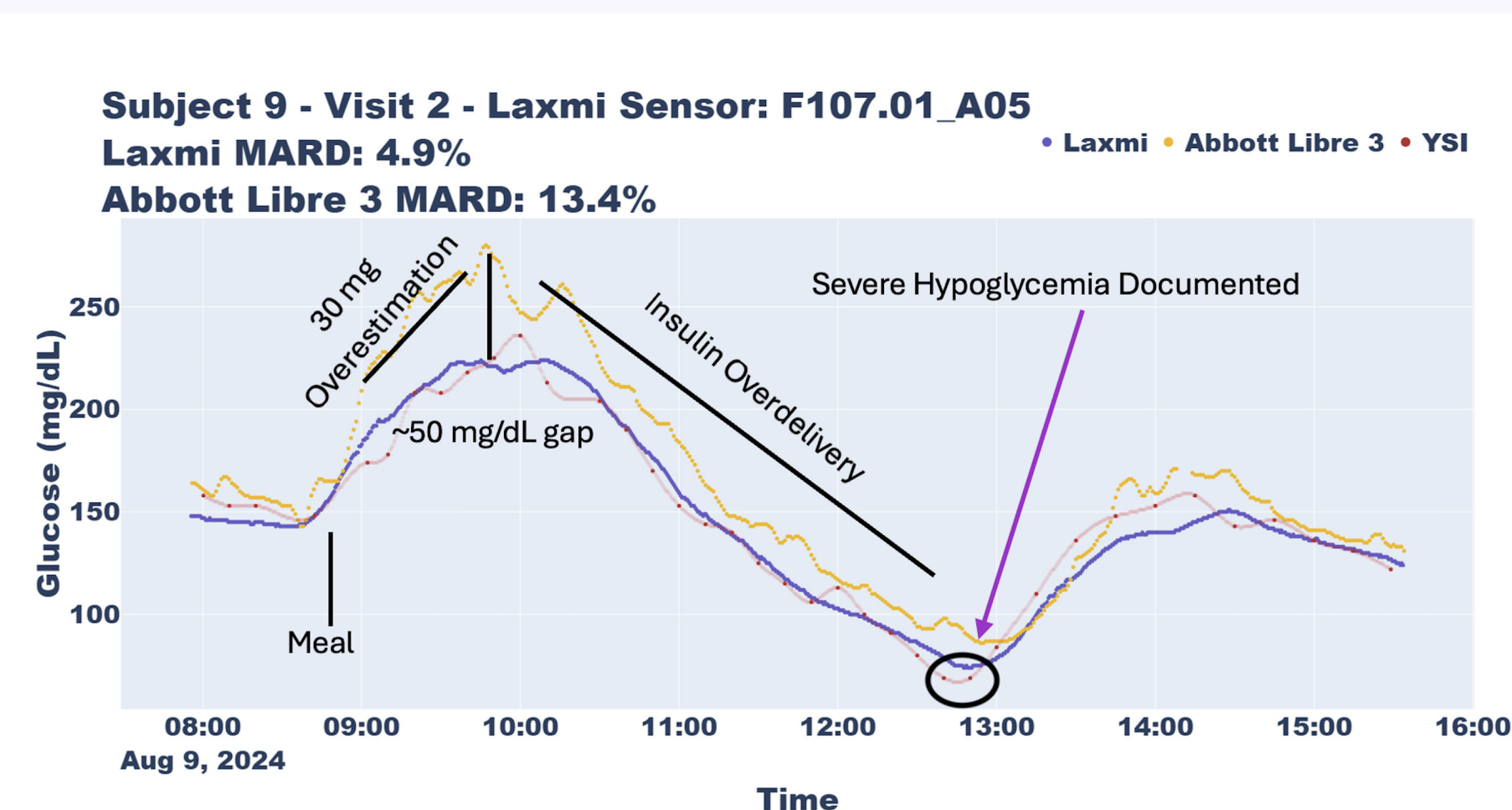


Figure 3: Real-World Example of CGM Overestimation, Leading to Insulin Overdosing and Severe Hypoglycemia

RESULTS

Using a YSI value as the first calibration point at each clinic visit, we evaluated the accuracy of the Laxmi sensor at low glucose levels against both comparators combined, all relative to the corresponding YSI measurements (Figure 4). Results showed that the Laxmi dermal sensors performed better against iCGM metrics, where it had more than twice as many results within the +/- 5 mg/dl range of the YSI and showed significantly better accuracy within +/- 10 and +/- 15 mg/dl ranges, demonstrating that dermal sensing could be of clinical superiority in detecting hypoglycemia, especially in the high-risk ranges.

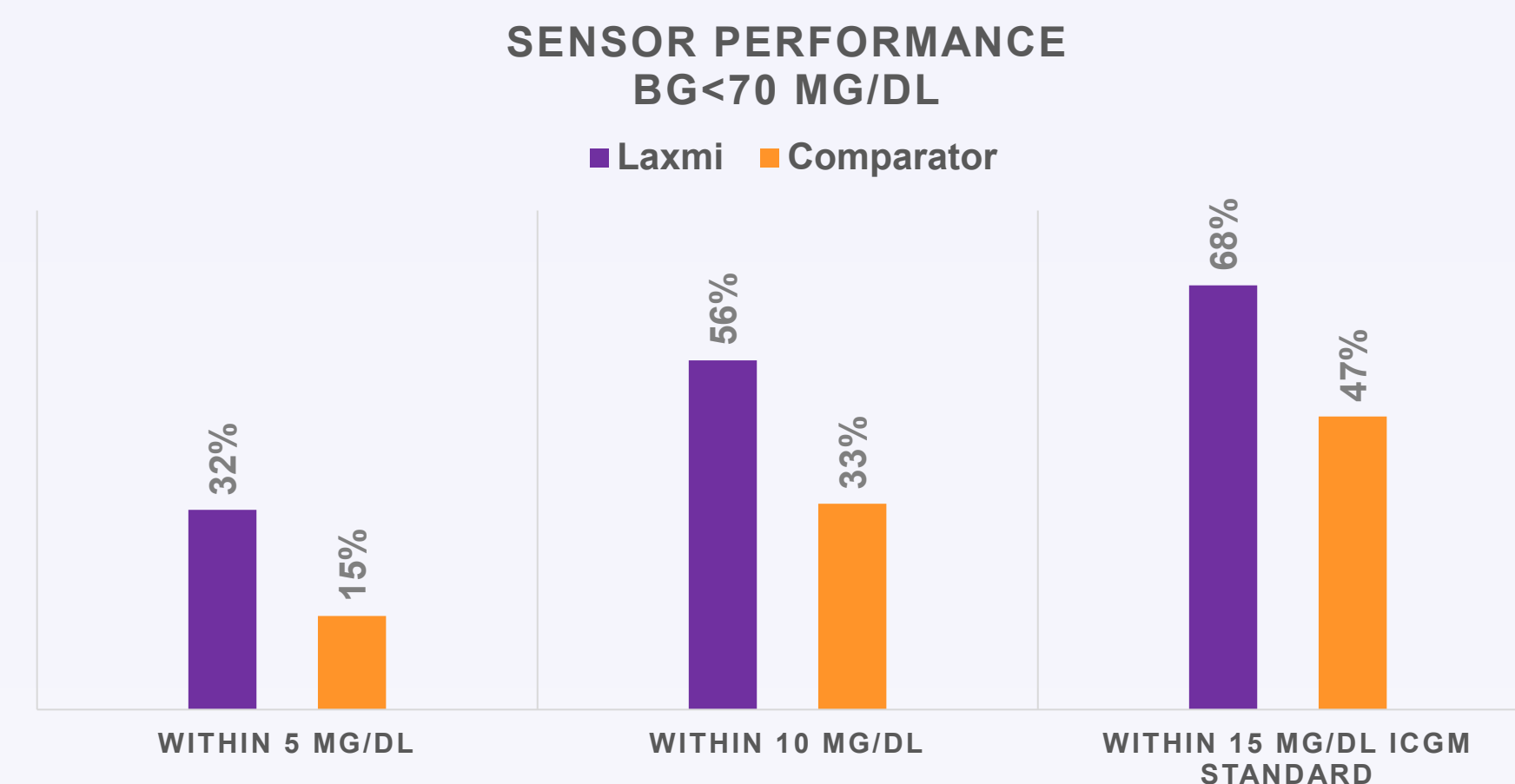


Figure 4: Comparison of Accuracy At Low Glucose Levels (N=92)

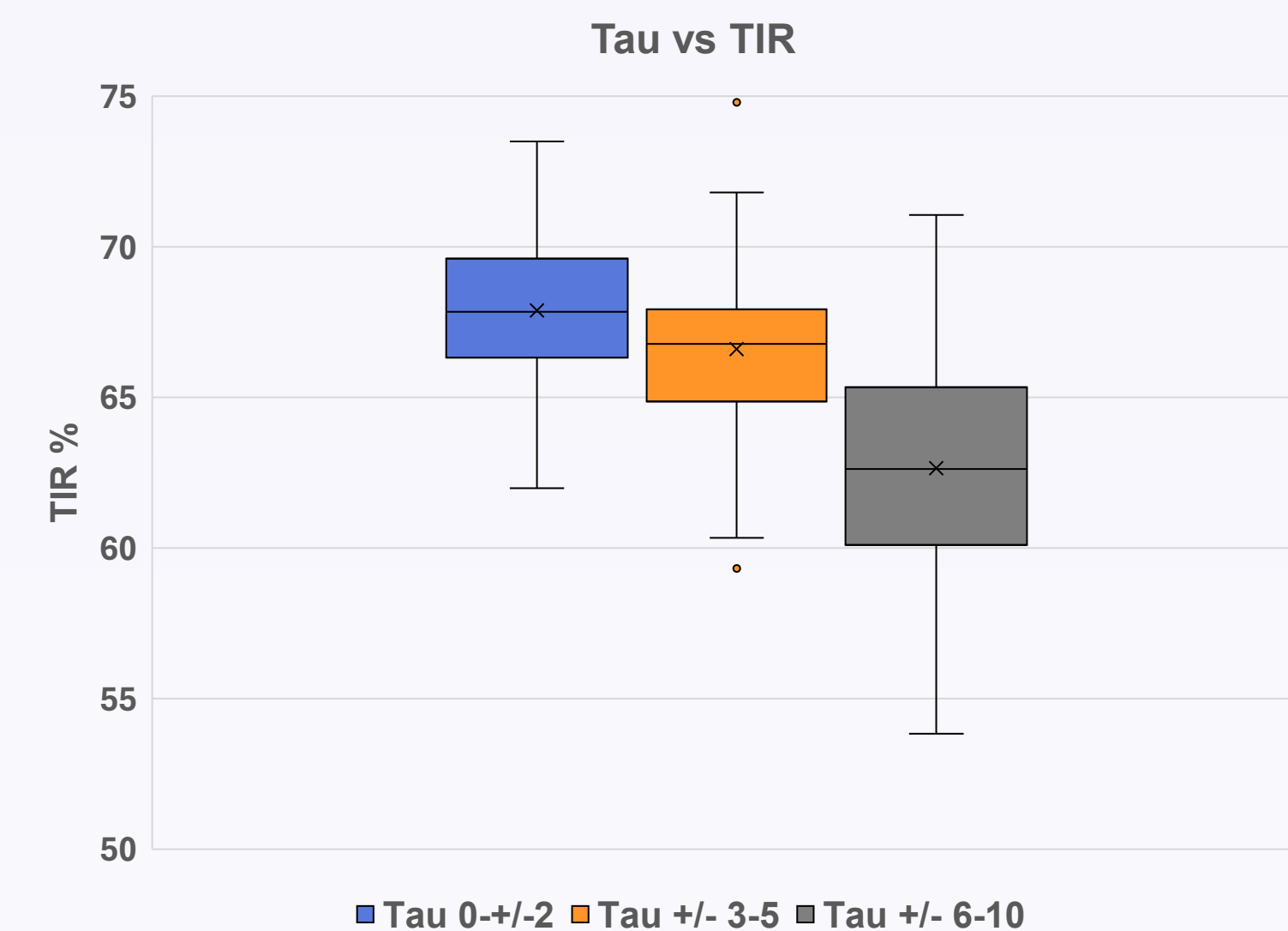


Figure 5: Tau's Effect on TIR

RESULTS

Using a well-accepted model (UVA type-1 diabetes simulator with open loop basal control and CGM based signals for prandial insulin delivery) to predict outcomes related to hypoglycemia and time in range, we evaluated the effect on TIR that a dermal sensor would have in comparison to traditional CGMs sensing the in the deep subcutaneous tissue (Figure 5). We observed the highest TIR % being associated with a tau of 0-2 min, with 8% improvement compared to the other CGMs. Results also showed that starting with a tau of ~6 min, the reduction in TIR is significant, and is much worse with a tau of +8 min. Figure 6 shows UVA-simulated data from 30 virtual adult patients (25 simulations for each patient with varying carbohydrate content). All patients were given the same meals under standardized conditions with a constant basal insulin rate, with correction boluses given only when triggered by the CGM signal. The data demonstrated once again that higher tau is associated with a reduction in TIR, highlighting the clinical relevance of CGM's tau in guiding insulin delivery.

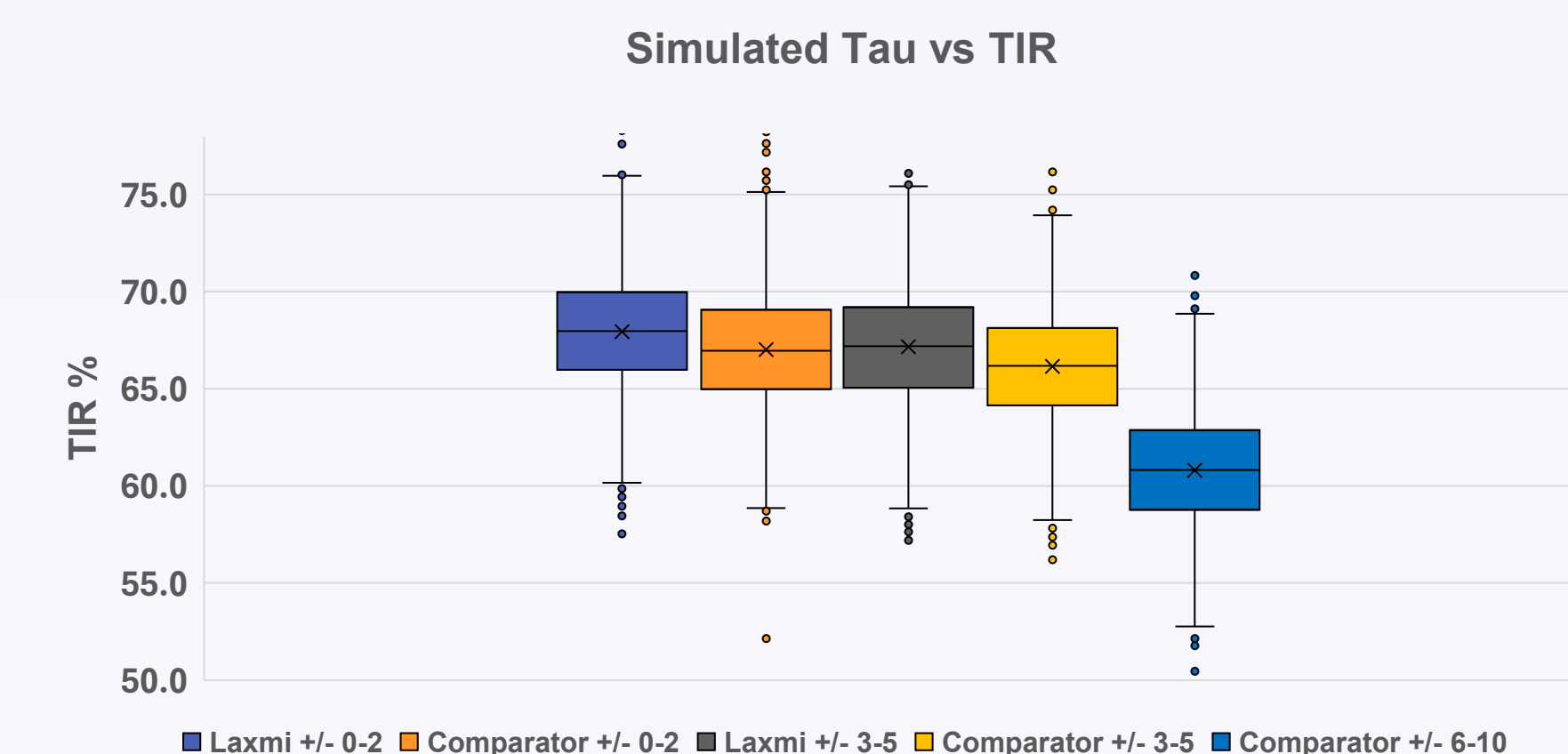


Figure 6: Simulated Tau vs TIR in 30 Adult Patients

CONCLUSION

We demonstrated that dermal sensing has a time lag close to 0, which could be associated with the highest TIR. Individuals with diabetes can have lower glucose targets with a system that eliminates fear of hypoglycemia. A dermal CGM could be a breakthrough that may lead to better outcomes, especially when integrated with feedback and control closed-loop systems, resulting in higher TIR and better control of diabetes.

FINANCIAL DISCLOSURE

None.