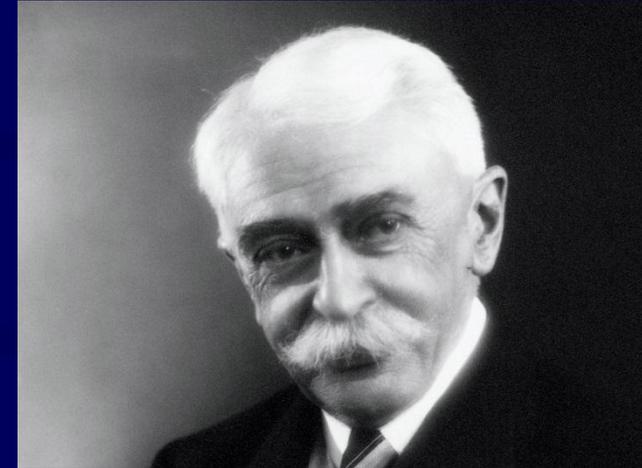


Perspectives d'Evolution de l'Insulinothérapie Automatisée



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Liens d'Intérêt



Eric Renard

Consultant/Orateur: A. Menarini Diagnostics, Abbott, Adelia Medical, Air Liquide SI, Astra-Zeneca, Asten, Bastide Médical, Becton-Dickinson, Boehringer-Ingelheim, Cellnovo, Dexcom Inc., Dinno-Santé, Eli-Lilly, Elivie, Hillo, Insulet Inc., Johnson & Johnson (Animas, LifeScan), Medtronic, Medirio, Nestlé Home Care, Novo-Nordisk, Orkyn, Roche, Sanofi-Aventis, VitalAire.

Soutiens pour la Recherche: Abbott, Dexcom Inc., Insulet Inc., Roche, Tandem.



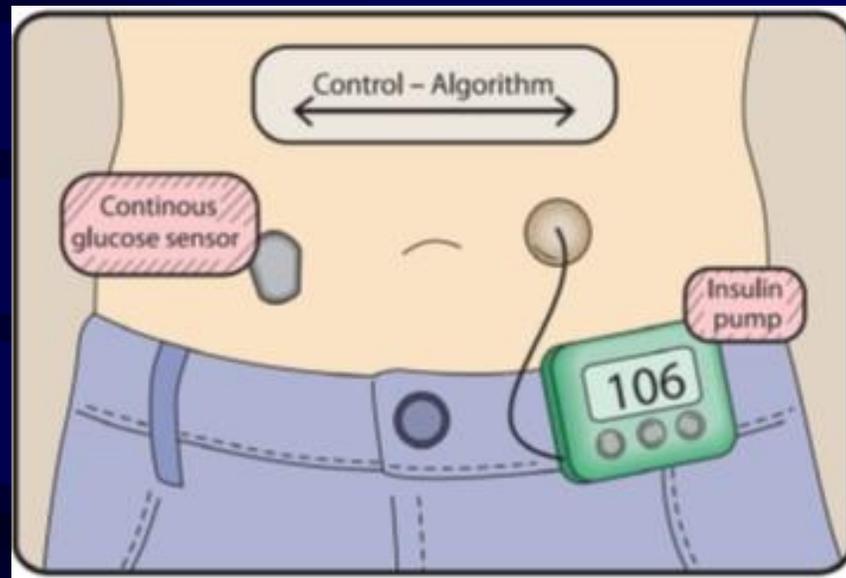
Limites Actuelles de la Boucle Fermée Hybride

Systèmes 'hybrides':

- Annonce des repas/comptage des glucides
- Annonce de l'activité physique
- Faible adaptabilité et individualisation

Capteurs sous-cutanés:

- Délai sang-interstitium
- Limités au glucose
- Exactitude limitée
- Calibration nécessaire



Insulinothérapie sous-cutanée:

- Délai d'action
- Hyperinsulinémie périphérique
- Modulation limitée de la perfusion par le volume d'éjection de la pompe

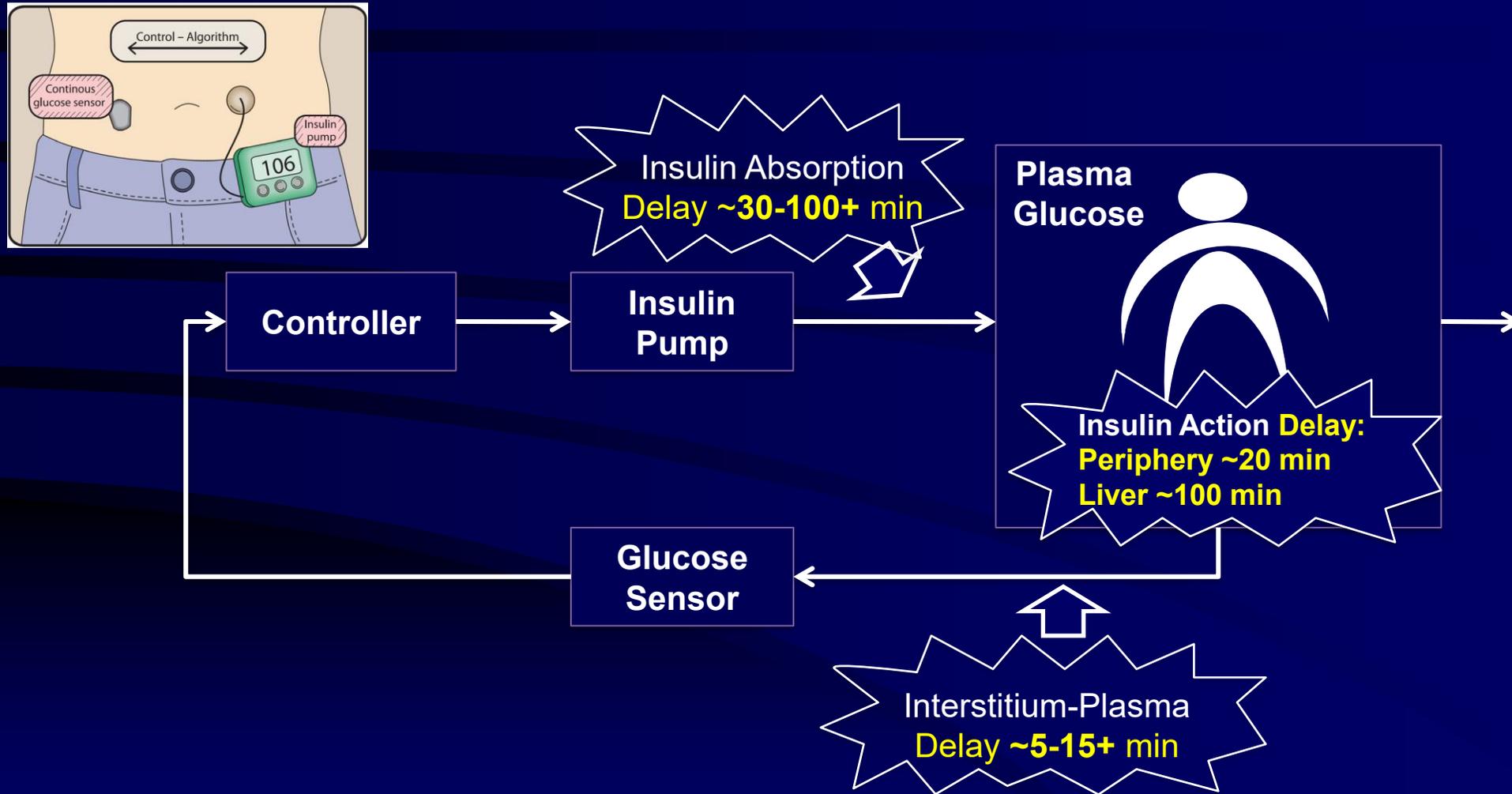
Dispositifs externes:

- Multiples (2-3)
- Visibles
- Tolérance cutanée

Dispositifs consommables

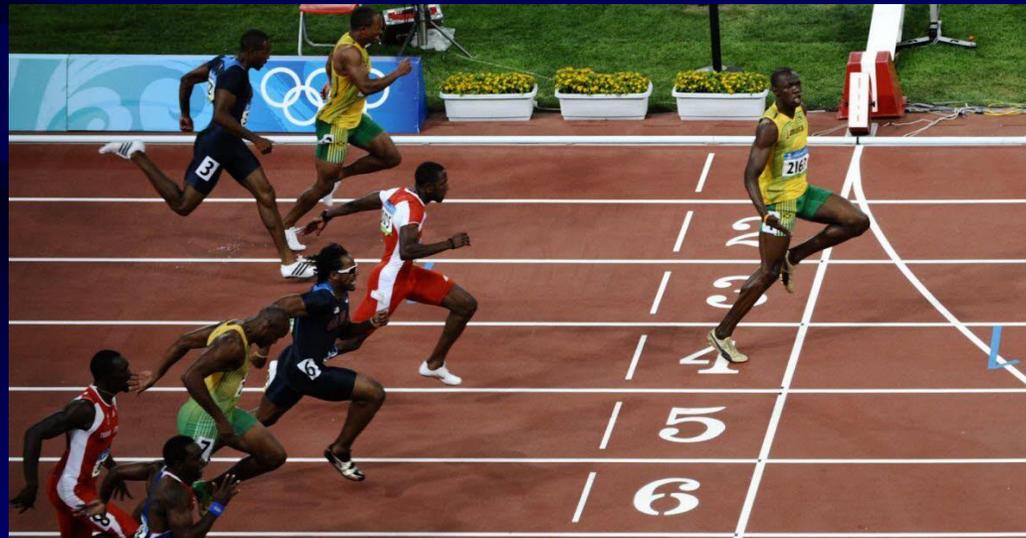
- Capteurs/7-14 jours
- Cathéters/3-7 jours
- Réservoirs/3 jours
- Déchets +/- recyclables

SC Glucose Sensing and SC Insulin Infusion A Key-Matter to Fix: Delays !

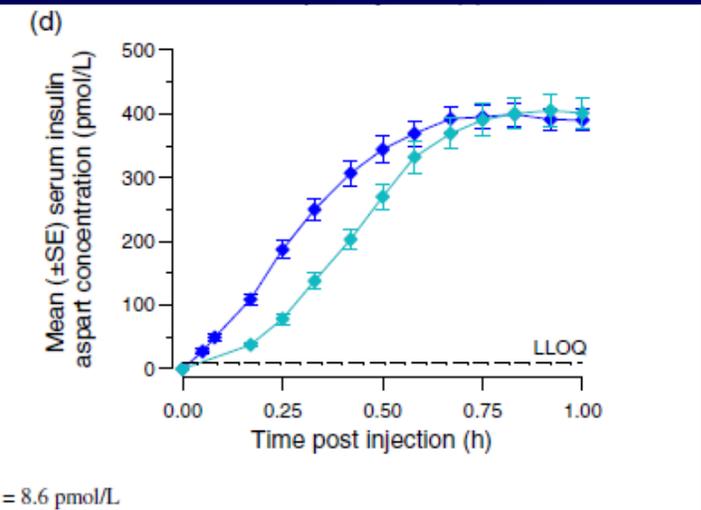
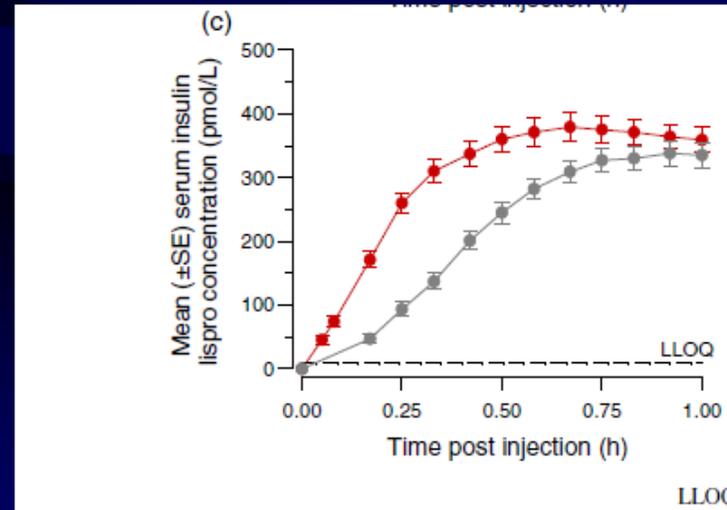
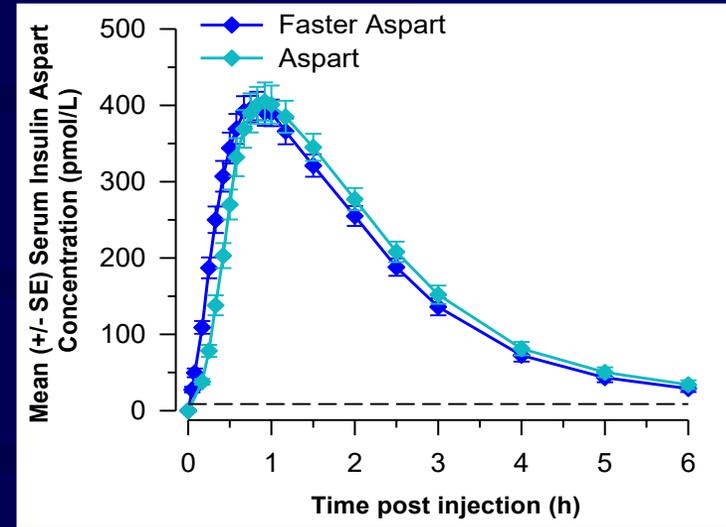
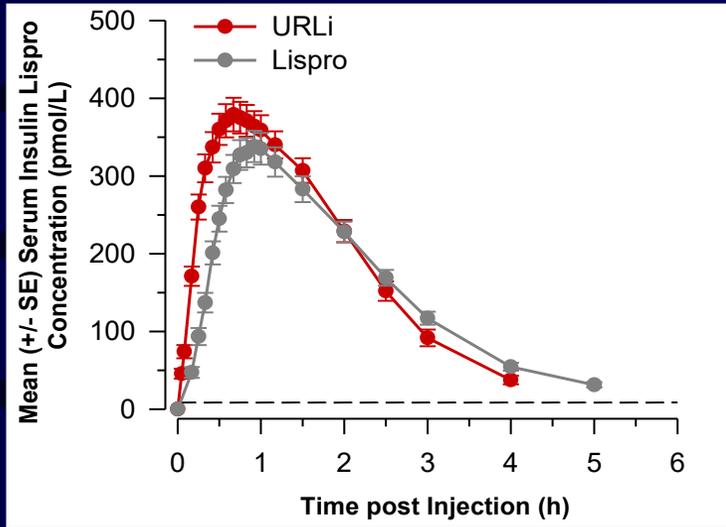


Projets d'Amélioration de l'Insulinothérapie Automatisée

- Accélérer l'action de l'insuline
- Synchroniser les variations glycémiques et l'action de l'insuline
- Accélérer la captation des variations glycémiques et l'action de l'insuline
- Combiner les améliorations vers un système plus physiologique



Ultra rapid lispro lowers postprandial glucose and more closely matches normal physiological glucose response compared to other rapid insulin analogues: A phase 1 randomized, crossover study



LLOQ = 8.6 pmol/L

FIGURE 1 Mean insulin lispro concentration (\pm SE) versus time post injection (A) and for the first hour post injection (C), mean insulin aspart concentration (\pm SE) versus time post injection (B) and for the first hour post injection (D) by treatment. LLOQ, lower limit of quantification

Fast Acting Insulin Aspart Compared with Insulin Aspart in the Medtronic 670G Hybrid Closed Loop System in Type 1 Diabetes: An Open Label Crossover Study



MiniMed 670G

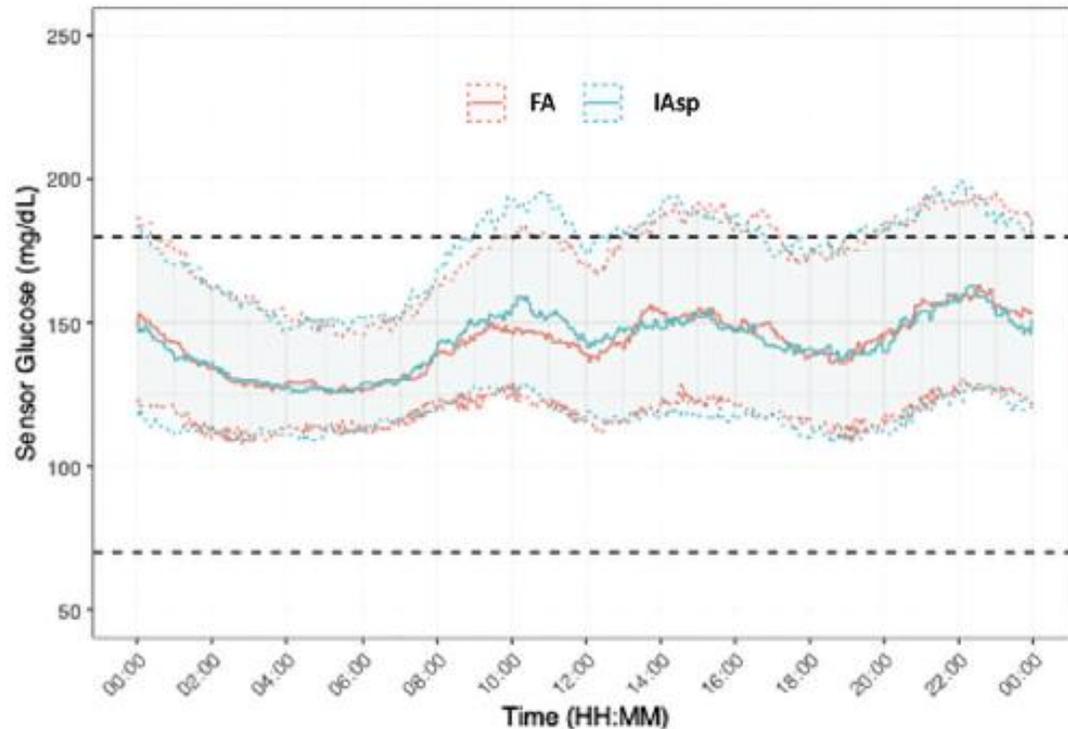
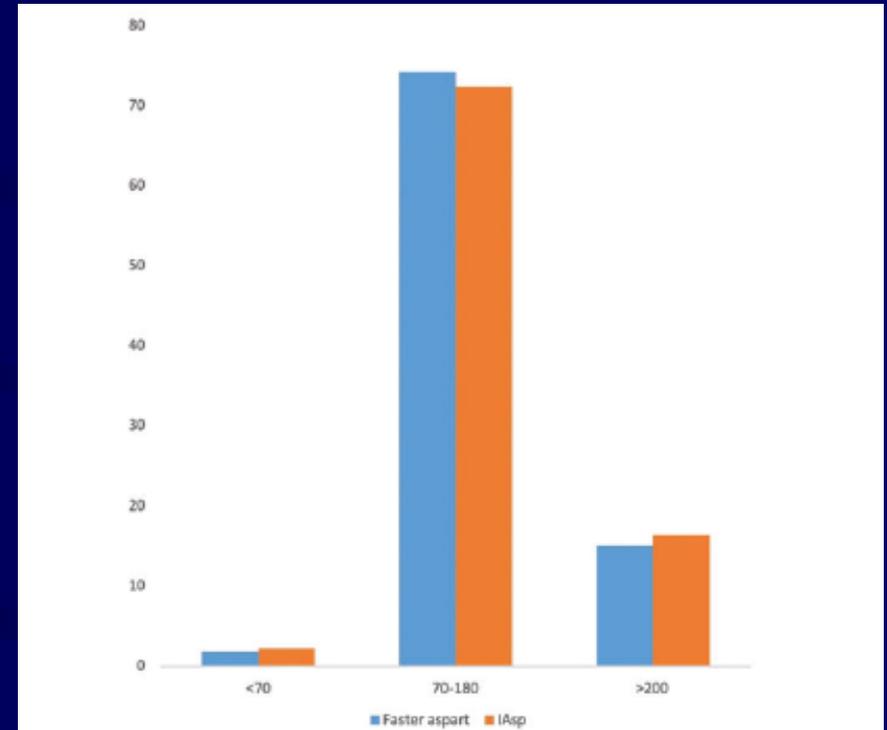


FIG. 4. Median sensor glucose levels for 24h. Continuous glucose monitor data covering weeks 3 through 7 of each treatment period aggregated across days and participants. Color images are available online.



	<70 mg/dL	70-180 mg/dL	>200 mg/dL
Percentage of time spent in range with FA relative to IAsp	-0.4% (p=0.029)	+1.81% (p=0.016)	-1.38% (p=0.016)

Profil de tolérance similaire pour les 2 insulines

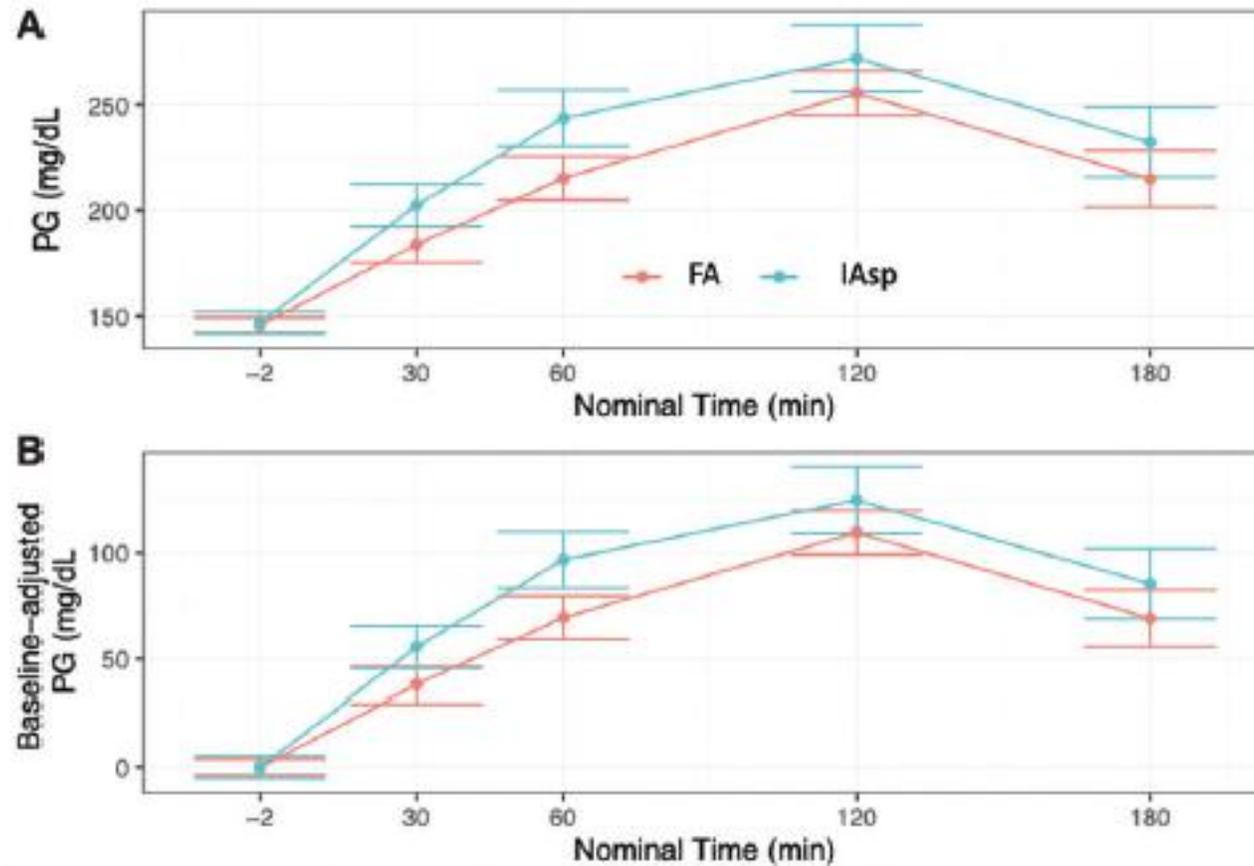


FIG. 2. Actual (A) and baseline-adjusted (B) PG levels over time after infusion with faster aspart or IAsp after a standardized meal test after 6 weeks of use of faster aspart versus IAsp. Error bars represent standard error of the mean. PG, plasma glucose. Color images are available online.

Moindre ascension de la glycémie après un repas-test sous Fast Aspart vs. Insuline Aspart

Fast-Acting Insulin Aspart Use with the MiniMed™ 670G System



MiniMed 670G

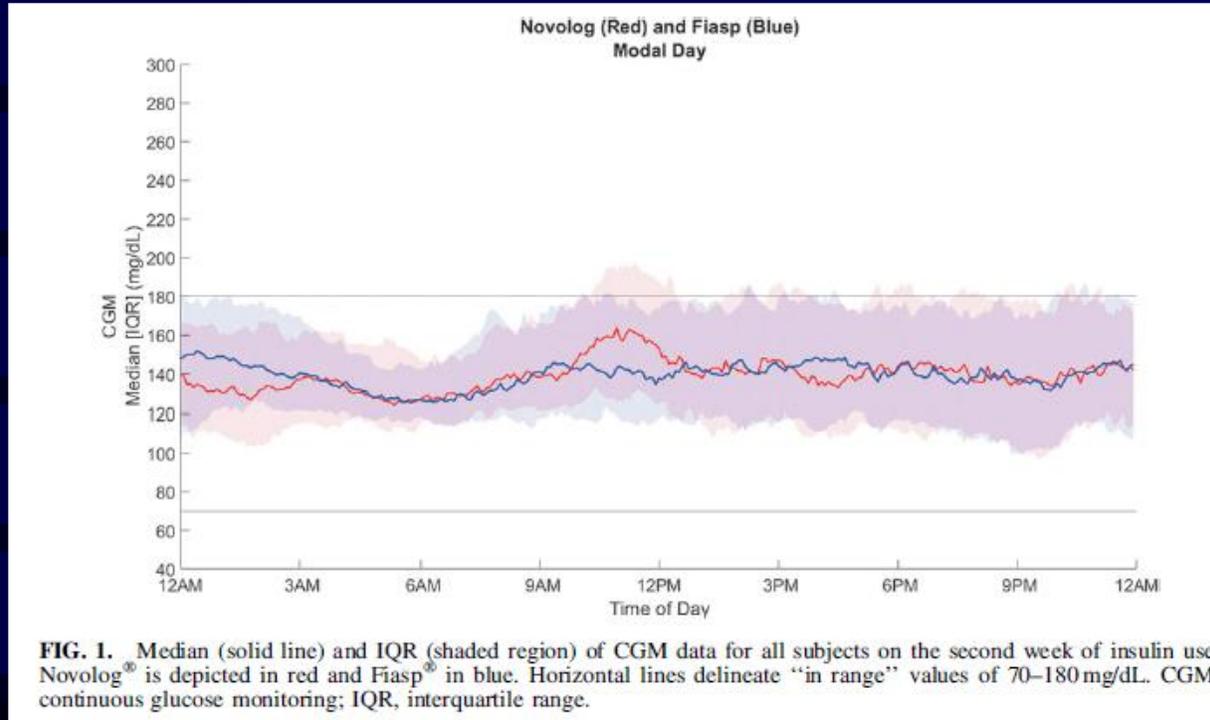


TABLE 2. DIFFERENCES IN DEPENDENT VARIABLES BETWEEN NOVOLOG AND FIASP

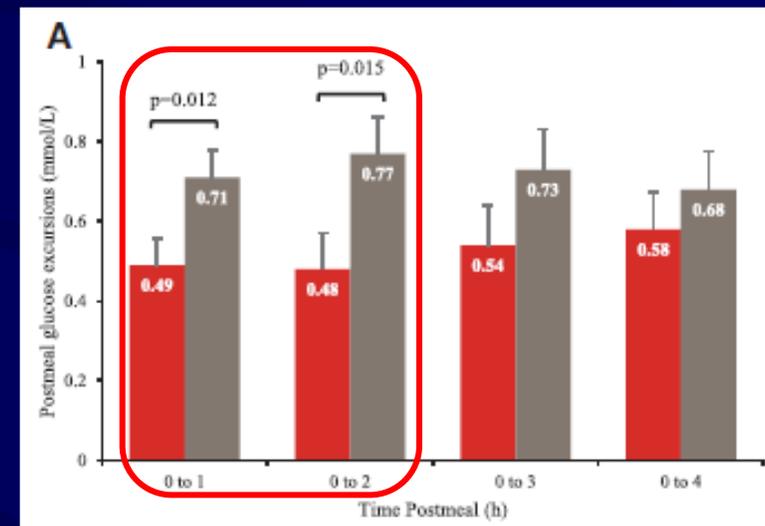
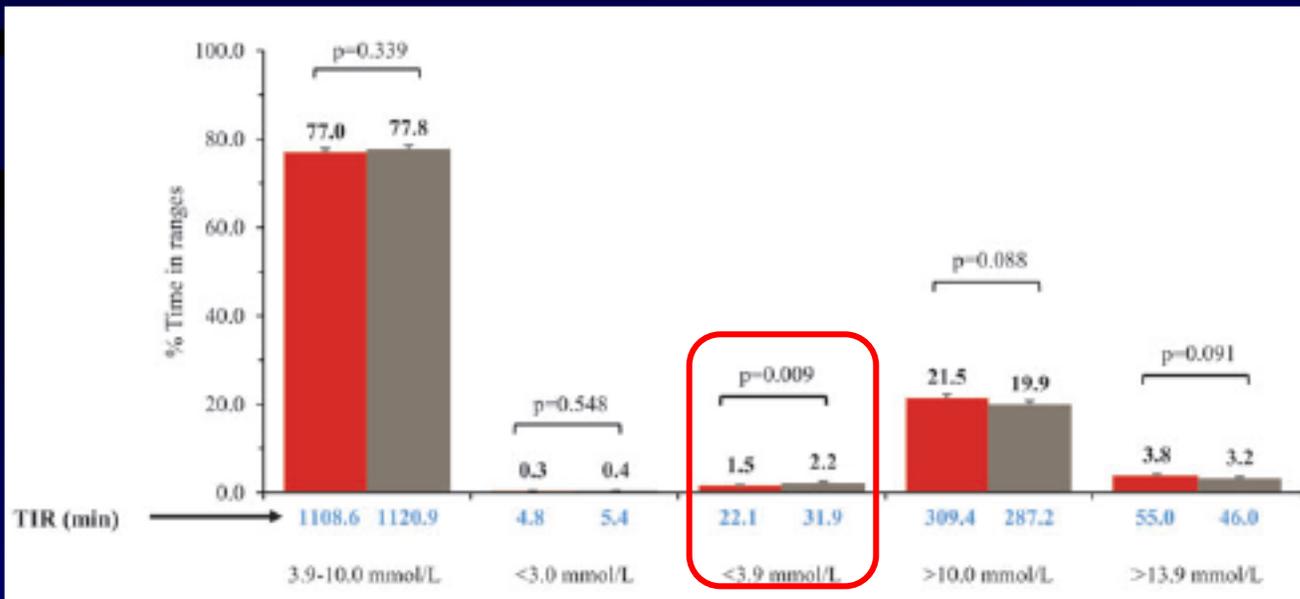
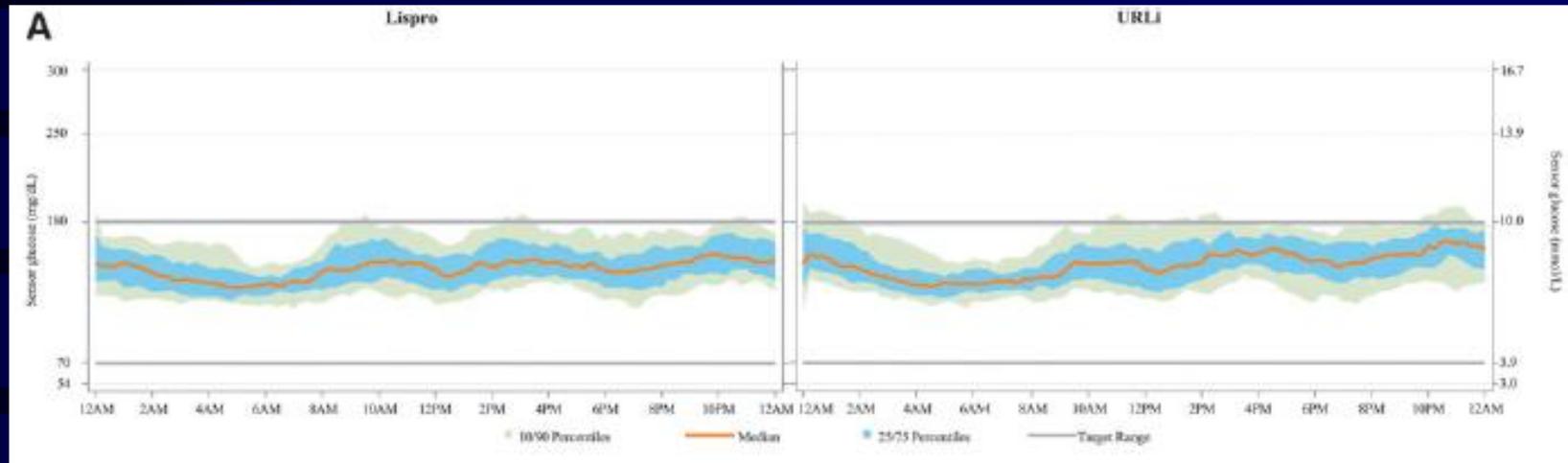
Dependent variable	Novolog [®] , ^a	Fiasp [®] , ^a	Difference (CI)	P
% time in range (70–180 mg/dL)	75.3 ± 9.5	78.4 ± 9.3	-3.1 (-6.3 to 0.02)	0.051
% time <70 mg/dL	3.1 ± 2.1	2.3 ± 2.0	0.8 (-0.4 to 2.1)	0.17
% time >180 mg/dL	21.6 ± 9.0	19.3 ± 8.9	2.2 (-1.1 to 5.6)	0.18
Glucose (mg/dL)	147 ± 12	146 ± 12	0.9 (-4.5 to 6.3)	0.74
% glucose coefficient of variation	28.6 ± 4.5	26.8 ± 4.4	1.8 (-0.1 to 3.7)	0.07
% time in auto mode	86.4 ± 9.2	84.4 ± 9.2	2.0 (-4.3 to 8.3)	0.52

^aLeast squares mean ± SD.
SD, standard deviation.

Ultrarapid Lispro Demonstrates Similar Time in Target Range to Lispro with a Hybrid Closed-Loop System



MiniMed 670G



Profil de tolérance similaire pour les deux insulines

Hybrid closed-loop glucose control with faster insulin aspart compared with standard insulin aspart in adults with type 1 diabetes: A double-blind, multicentre, multinational, randomized, crossover study



Cam APS FX

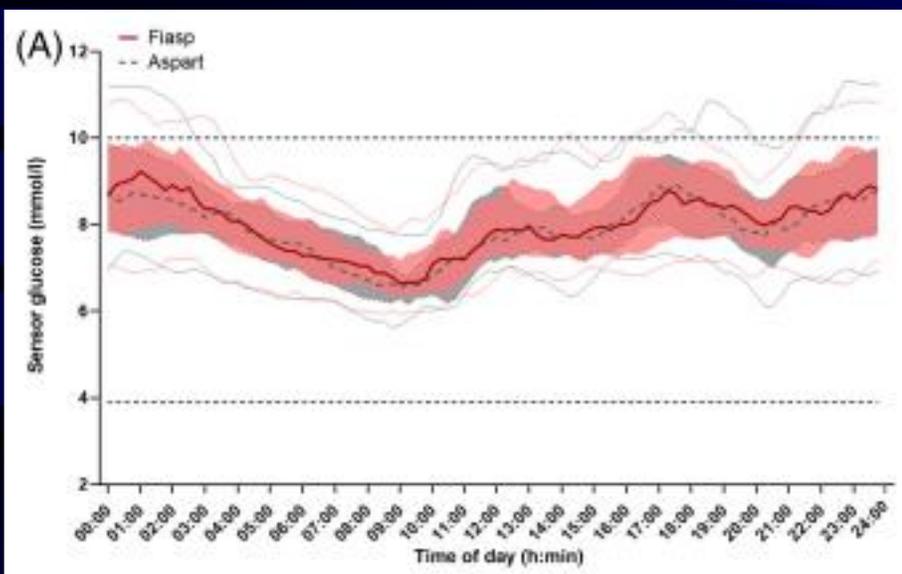


TABLE 2 Glucose control and insulin delivery over 8 weeks of closed-loop with faster-acting insulin (Fiasp) and closed-loop with standard insulin aspart

	Fiasp (n = 25)	Standard insulin aspart (n = 25)	p value	95% CI for treatment difference
% of time with sensor glucose level				
3.9 to 10.0 mmol/L*	75 ± 8	75 ± 8	<.001**	-0.6 (-1.8, 0.7)
<3.9 mmol/L	2.4 (1.2, 3.2)	2.9 (1.7, 4.0)	.01	-0.3 (-0.5, -0.1)
<3.5 mmol/L	1.2 (0.5, 1.9)	1.7 (0.7, 2.3)	.02	-0.3 (-0.5, -0.1)
<3.0 mmol/L	0.4 (0.2, 0.7)	0.7 (0.2, 0.9)	.03	-0.3 (-0.6, -0.1)
<2.8 mmol/L	0.2 (0.1, 0.4)	0.4 (0.1, 0.5)	.01	-0.4 (-0.6, -0.1)
>10.0 mmol/L	22 ± 9	21 ± 9	.13	1.2 (-0.2, 2.5)
>16.7 mmol/L	1.4 (0.4, 2.1)	1.2 (0.5, 1.6)	.94	0.0 (-0.2, 0.2)
Mean glucose (mmol/L)	8.1 ± 0.8	8.0 ± 0.8	.13	0.10 (-0.02, 0.22)
Glucose SD (mmol/L)	2.9 ± 0.5	2.9 ± 0.5	.90	-0.00 (-0.08, 0.07)
Glucose CV (%)	36 ± 4	36 ± 4	.18	-0.5 (-1.3, 0.2)
Low blood glucose index	0.7 (0.5, 1.0)	0.9 (0.5, 1.1)	.01	-0.3 (-0.5, -0.1)
Total daily insulin (units/day)	49 ± 15	49 ± 15	.45	0.6 (-1.0, 2.3)
Total daily basal insulin (units/day)	30 ± 13	29 ± 13	.14	1.3 (-0.3, 2.8)
Total daily bolus insulin (units/day)	19 ± 7	19 ± 6	.93	0.1 (-1.2, 1.3)
% time using closed-loop	95 (94, 97)	96 (92, 97)	.98	0.1 (-0.6, 0.6)
% time using CGM	97 (96, 98)	97 (95, 98)	-	-

Hybrid Closed-Loop with Faster Insulin Aspart Compared with Standard Insulin Aspart in Very Young Children with Type 1 Diabetes: A Double-Blind, Multicenter, Randomized, Crossover Study



Cam APS FX

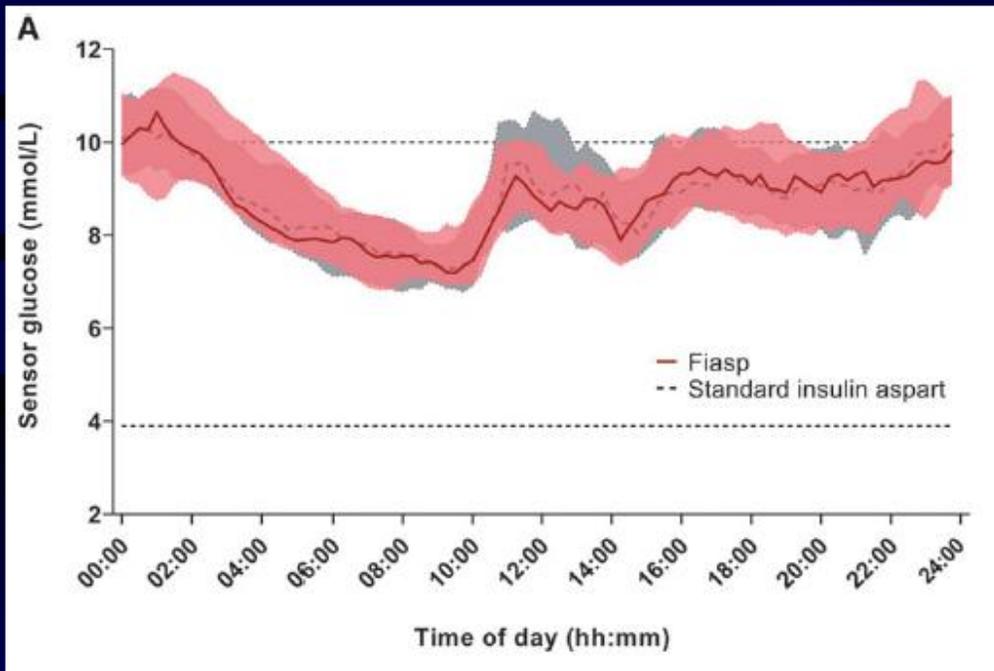


TABLE 1. GLUCOSE CONTROL AND INSULIN DELIVERY OVER 8 WEEKS OF CLOSED-LOOP WITH FASTER-ACTING INSULIN ASPART AND CLOSED-LOOP WITH STANDARD INSULIN ASPART

	<i>Fiasp</i> (n=25)	<i>Standard IAsp</i> (n=25)	Mean adjusted difference (95% CI) ^a	P ^c
Percent of time with sensor glucose level				
3.9–10.0 mmol/L ^b	64.2±8.8	64.6±8.8	-0.33 (-2.13 to 1.47)	0.71
<3.9 mmol/L	3.5 (2.6, 6.3)	3.7 (2.6, 6.2)	-0.05 (-0.43 to 0.34)	0.81
<3.5 mmol/L	2.0 (1.3, 4.2)	2.0 (1.4, 4.0)	-0.06 (-0.34 to 0.22)	0.68
<3.0 mmol/L	0.8 (0.5, 1.8)	0.8 (0.4, 1.9)	0.01 (-0.14 to 0.16)	0.92
>10.0 mmol/L	31.3±9.0	31.0±8.9	0.26 (-1.60 to 2.11)	0.78
>16.7 mmol/L	4.5 (2.2, 6.6)	4.1 (1.7, 7.7)	-0.16 (-0.78 to 0.46)	0.60
Mean glucose (mmol/L)	8.9±0.9	8.9±0.8	0.03 (-0.16 to 0.21)	0.78
Glucose SD (mmol/L)	3.7±0.6	3.7±0.6	0.02 (-0.12 to 0.16)	0.76
Glucose CV (%)	42.0±4.6	41.9±4.7	0.12 (-1.09 to 1.32)	0.85
Total daily insulin (units/kg/day)	0.74±0.12	0.72±0.12	0.03 (0.00 to 0.07)	0.04
Total daily basal insulin (units/kg/day)	0.38±0.10	0.35±0.10	0.03 (0.00 to 0.06)	0.04
Total daily bolus insulin (units/kg/day)	0.37±0.09	0.37±0.10	0.00 (-0.01 to 0.02)	0.71
% time using closed-loop	96.4 (91.7, 97.9)	96.7 (95.0, 98.0)	—	—
% time using CGM	97.8 (96.2, 98.3)	97.9 (96.0, 98.6)	—	—

Pas d'hypoglycémie sévère ni d'acido-cétose ni d'évènement indésirable grave pendant l'étude

CamAPS FX Hybrid Closed-Loop with Ultra-Rapid Lispro Compared with Standard Lispro in Adults with Type 1 Diabetes: A Double-Blind, Randomized, Crossover Study



Cam APS FX

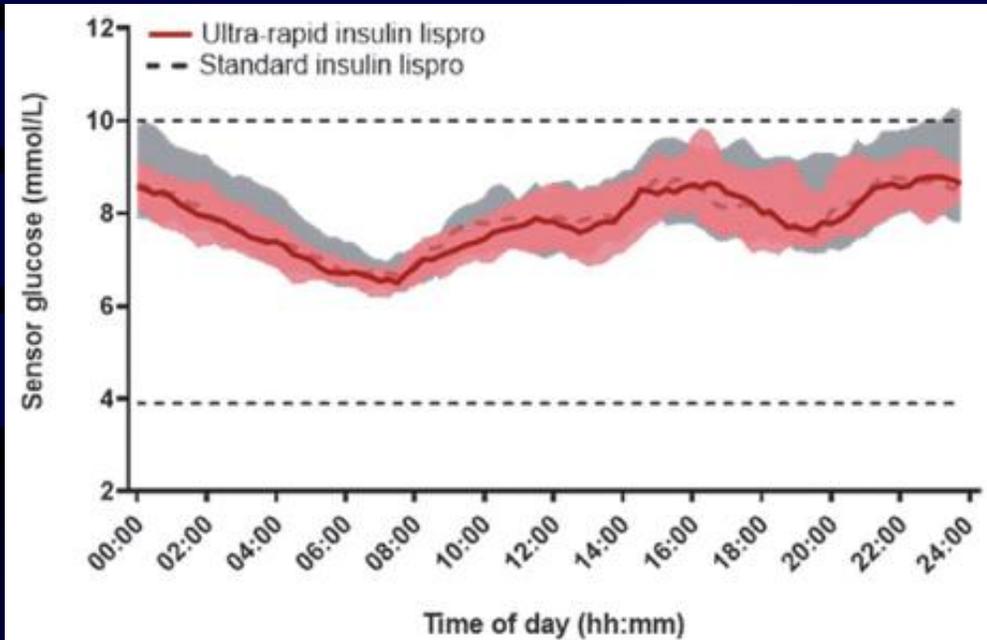


TABLE 2. GLUCOSE CONTROL AND INSULIN DELIVERY OVER 8 WEEKS OF CLOSED-LOOP WITH FASTER-ACTING INSULIN LISPRO AND CLOSED-LOOP WITH STANDARD INSULIN LISPRO

	Ultra-rapid insulin lispro (n=26)	Standard insulin lispro (n=27)	p ^b	95% CI for treatment difference ^b
Percent of time with sensor glucose level				
3.9 to 10.0 mmol/L ^a [70–180 mg/dL]	78.7±9.8	76.2±9.6	0.005	2.52 (0.82 to 4.23)
<3.9 mmol/L [<70 mg/dL]	2.3 (1.3, 2.7)	2.1 (1.4, 3.3)	0.327	-0.11 (-0.34 to 0.12)
<3.0 mmol/L [<54 mg/dL]	0.30 (0.15, 0.46)	0.30 (0.16, 0.46)	0.650	-0.01 (-0.06 to 0.04)
>10.0 mmol/L [>180 mg/dL]	19.2±9.9	21.5±10.1	0.011	-2.38 (-4.18 to -0.59)
>16.7 mmol/L [>300 mg/dL]	0.8 (0.2, 2.0)	1.1 (0.3, 3.5)	0.083	-0.43 (-0.93 to 0.06)
Mean glucose (mmol/L)	7.9±0.8	8.1±0.9	0.048	-0.17 (-0.33 to -0.00)
Mean glucose (mg/dL)	142±14	146±16		-3.1 (-5.9 to -0.0)
Glucose SD (mmol/L)	2.8±0.7	2.9±0.6	0.098	-0.10 (-0.22 to 0.02)
Glucose SD (mg/dL)	50±13	52±11		-1.8 (-4.0 to 0.4)
Glucose CV (%)	34.7±5.0	35.5±4.6	0.279	-0.56 (-1.61 to 0.48)
Total daily insulin (U/day)	41.7 (32.6, 54.7)	42.8 (31.3, 53.4)	0.502	-0.57 (-2.28 to 1.15)
Total daily basal Insulin (U/day)	26.4 (20.2, 38.5)	28.6 (16.9, 34.6)	0.814	-0.19 (-1.85 to 1.47)
Total daily bolus Insulin (U/day)	15.0 (11.3, 19.3)	15.3 (10.3, 20.7)	0.822	0.11 (-0.86 to 1.08)
% time using closed-loop	96.8 (95.4, 97.6)	96.5 (94.7, 98.0)	0.714	0.11 (-0.49 to 0.70)
% time using CGM	98.5 (98.1, 98.9)	98.6 (98.2, 98.9)	0.451	-0.09 (-0.35 to 0.16)

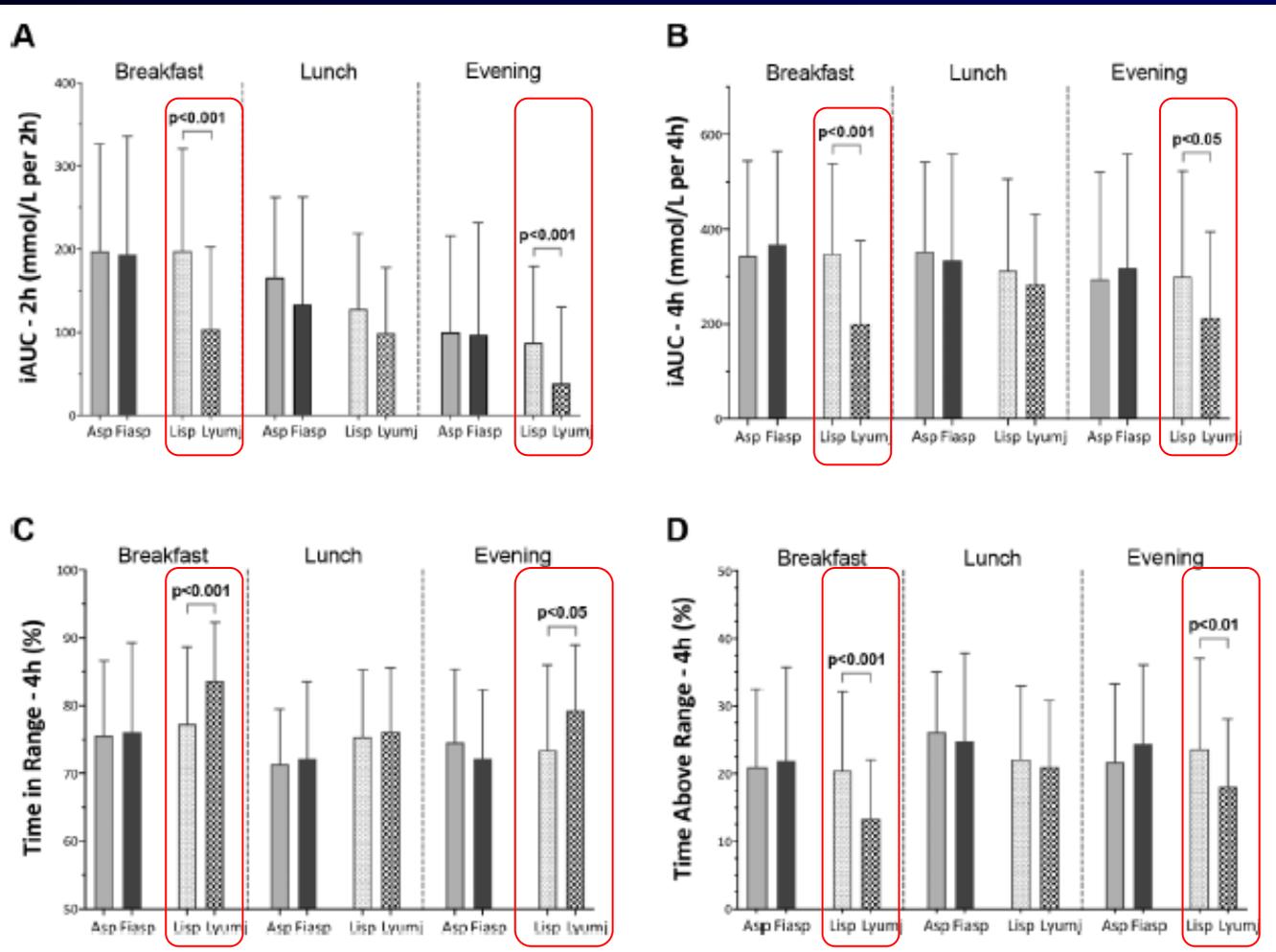
*Pas d'hypoglycémie sévère et pas d'acido-cétose.
Plus d'évènements indésirables au site de perfusion avec URLi
mais toujours d'intensité faible à modérée*

Postprandial Glucose Excursions with Ultra-Rapid Insulin Analogues in Hybrid Closed-Loop Therapy for Adults with Type 1 Diabetes



Cam APS FX

Moins d'hyperglycémie postprandiale, plus de temps dans la cible 70-180 mg/dL et moins de temps > 180 mg/dL dans les 4h postprandiales avec URli vs. Lispro au petit-déjeuner et au dîner



Diabetes Technology and Therapeutics

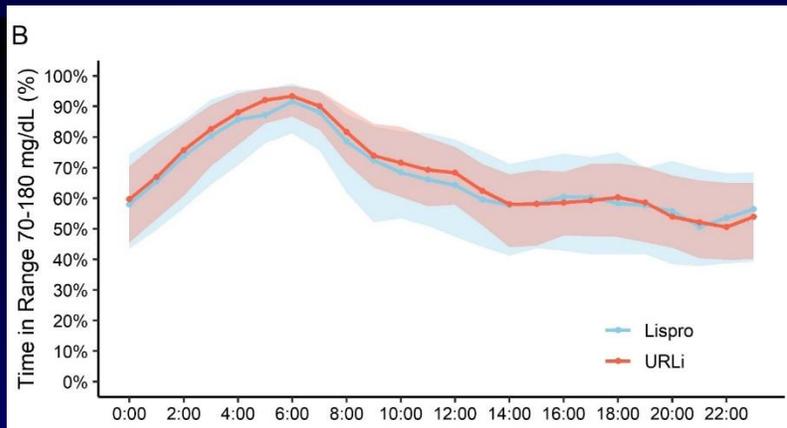
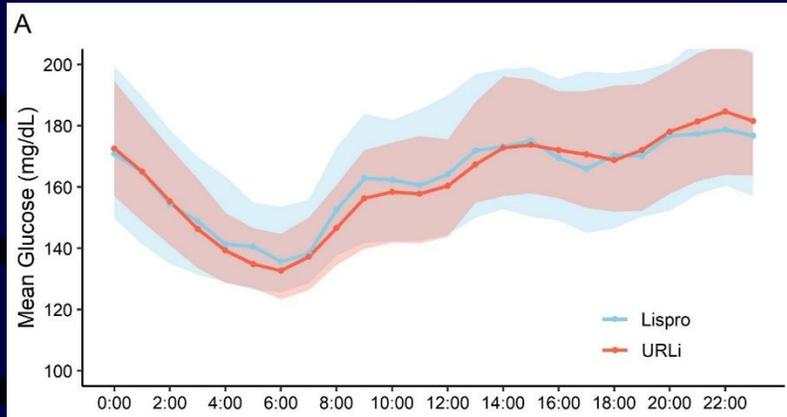
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DOI: 10.1089/dia.2023.0509

High Satisfaction with Control-IQ 1.5 and Ultra-Rapid Lispro Insulin in Children, Adolescents and Adults with Type 1 Diabetes



Tandem Control-IQ



	Lispro Period (N=179) MEAN ± SD	URLi Period (N=179) MEAN ± SD	Mean Difference (95% CI) [P-VALUE]
Time <54 mg/dL (<3.0 mmols/L) (%)	0.27% ± 0.35%	0.26% ± 0.27%	-0.02% (-0.05%, 0.02%) [0.41]
Time <70 mg/dL (<3.9 mmols/L) (%)	1.4% ± 1.3%	1.2% ± 1.0%	-0.2% (-0.3%, -0.1%) [<0.001]
CGM Hypoglycemic Event Rate per Week ^a	0.46 ± 0.75	0.49 ± 0.55	0.01 (-0.09, 0.10) [0.88]
Time 70-180 mg/dL (3.9 – 10.0 mmols/L) (%)	65% ± 15%	67% ± 13%	2% (1%, 3%) [0.004]
Time 70-140 mg/dL (3.9 – 7.8 mmols/L) (%)	40% ± 14%	42% ± 13%	2% (1%, 3%) [0.005]
Time >180 mg/dL (>10.0 mmols/L) (%)	34% ± 15%	32% ± 13%	-2% (-3%, 0%) [0.01]
Time >250 mg/dL (>13.9 mmols/L) (%)	12% ± 10%	11% ± 8%	-1% (-2%, 0%) [0.01]
Mean Glucose (mg/dL)	167 ± 26	165 ± 23	-2 (-4, 0) [0.03]
Glucose SD (mg/dL)	61 ± 15	60 ± 14	-1 (-2, 0) [0.08]
Glucose CV (%)	36% ± 5%	36% ± 5%	-0% (-1%, 0%) [0.51]
CGM Hyperglycemic Event Rate per Week ^b	1.8 ± 1.9	1.6 ± 1.6	-0.1 (-0.3, 0.1) [0.17]

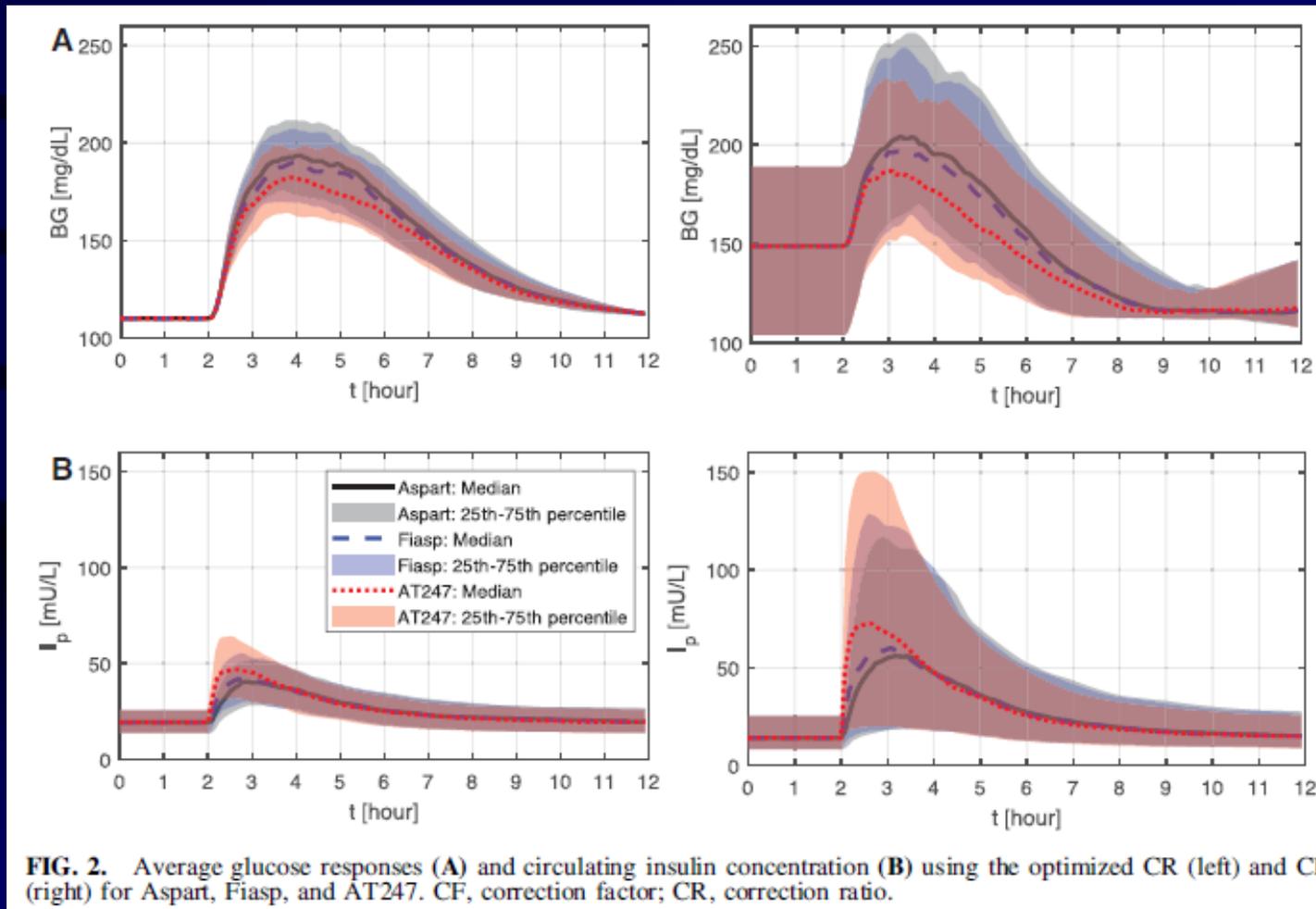
	Overall	End of Lispro Lead-in N=173 mean ± SD	End of URli Lead-in N=172 mean ± SD	Mean Difference (95% CI) [P-value] ^a
HbA1c (%)		7.1 ± 0.9	7.0 ± 0.8	-0.1 (-0.2, 0.0) [0.01]
[mmol/mol]		54 ± 9	53 ± 9	-1.1 (-1.9, -0.3)
		Peds (6-17)		Adults (18+)
		End of Lispro Lead-in N=103 mean ± SD	End of URli Lead-in N=107 mean ± SD	End of Lispro Lead-in N=70 mean ± SD
		End of URli Lead-in N=65 mean ± SD		
HbA1c (%)		7.2 ± 0.9	7.1 ± 0.8	6.9 ± 0.8
[mmol/mol]		55 ± 10	54 ± 9	52 ± 8

3 Hypoglycémies sévères avec URli
Pas d'acidocétose (critère primaire composite)

Maximizing Glycemic Benefits of Using Faster Insulin Formulations in Type 1 Diabetes: In Silico Analysis Under Open- and Closed-Loop Conditions



Jenny L. Diaz C., PhD, Patricio Colmegna, PhD, and Marc D. Breton, PhD



L'optimisation *in silico* des ratios insuline/carbs (CR) et facteur de correction (CF) améliore la glycémie postprandiale avec Fiasp et AT247

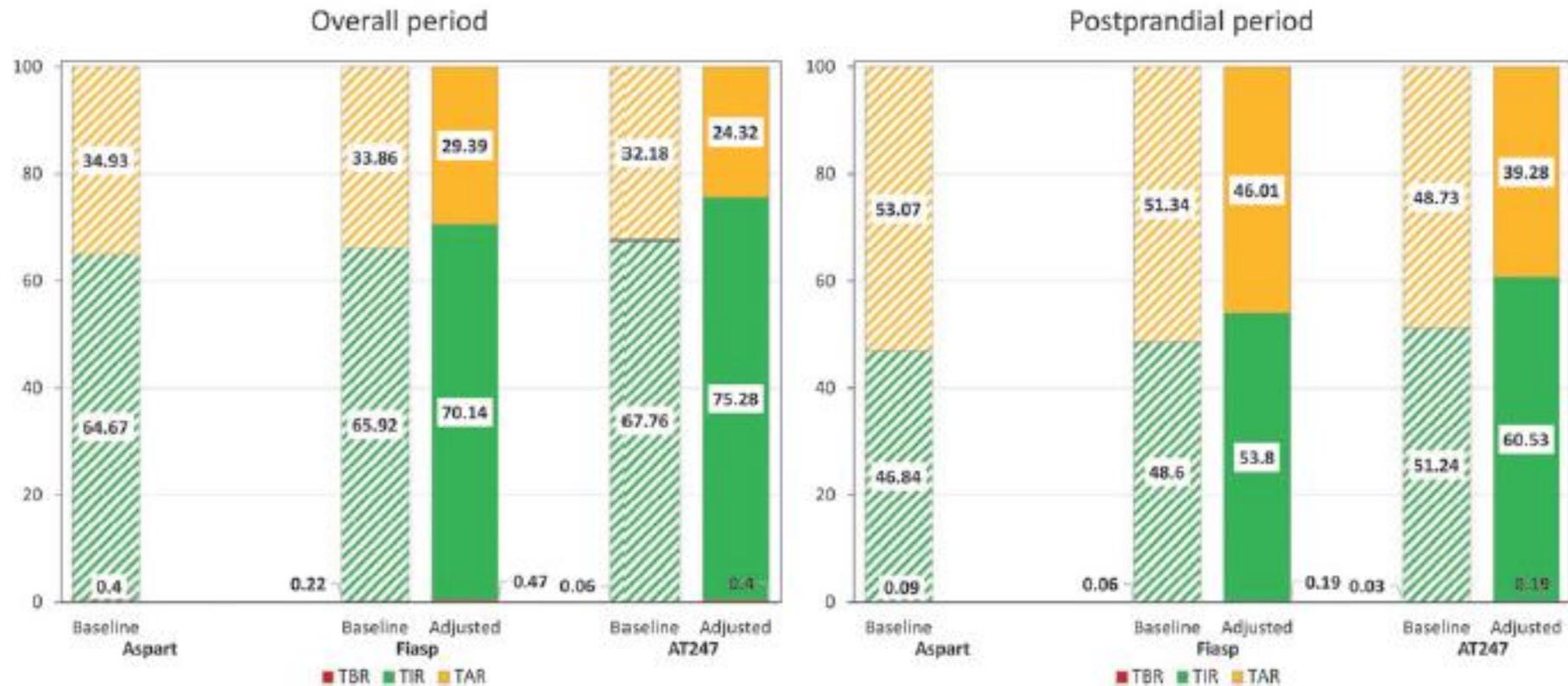


FIG. 4. Glycemic metrics for the full closed-loop insulin therapy (RocketAP) under baseline (striped) and adjusted (solid) scenario for overall (left) and postprandial (right) periods.

Projets d'Amélioration de l'Insulinothérapie Automatisée

- Accélérer l'action de l'insuline
- Synchroniser les variations glycémiques et l'action de l'insuline
- Accélérer la captation des variations glycémiques
- Combiner les améliorations vers un système plus physiologique

Adjuvant Liraglutide and Insulin Versus Insulin Monotherapy in the Closed-Loop System in Type 1 Diabetes: A Randomized Open-Labelled Crossover Design Trial

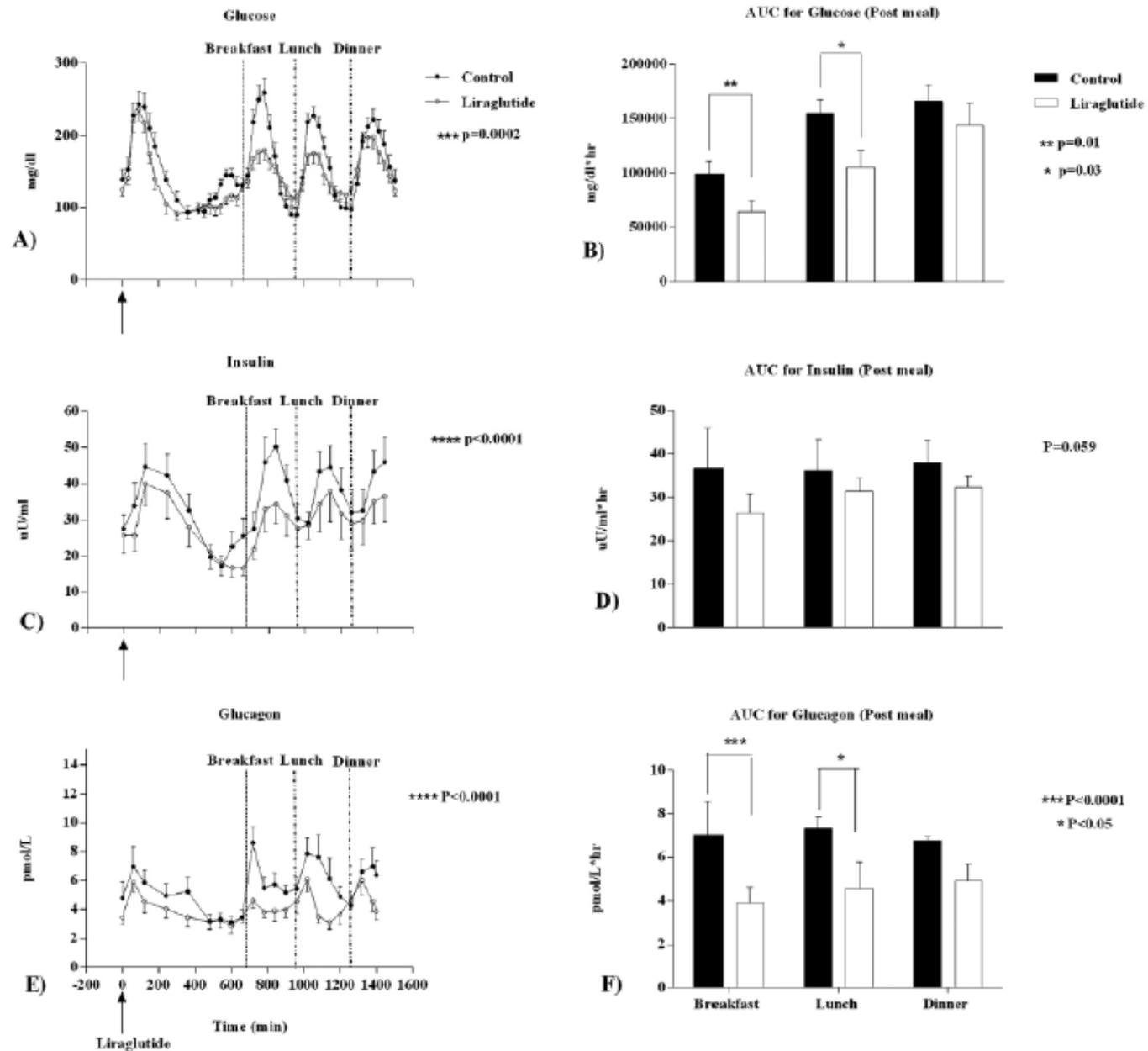


Figure 2. Glucose, insulin and glucagon concentrations in CL with and without liraglutide (A, C, and E) and area under curve values following postprandial changes in glucose, insulin, and glucagon with meals (B, D, and F). Glucose, insulin, and glucagon concentrations (A, C, and E) were analyzed during the time points 0-1440 minutes and are represented as black circles for control and white circles for treatment (liraglutide). AUC for glucose, insulin, and glucagon (B, D, and F) were calculated postprandial 2 hours after each meal (660-780 minutes after breakfast, 960-180 minutes after lunch, and 1260-1380 minutes after dinner) and are represented as black bars for control and white bars for treatment (liraglutide). All data are expressed as mean \pm SD. The difference between the treatment vs control arm is expressed as mean \pm 95% confidence interval (CI). A P value $< .05$ was considered to be statistically significant.

A Novel Dual-Hormone Insulin-and-Pramlintide Artificial Pancreas for Type 1 Diabetes: A Randomized Controlled Crossover Trial

Diabetes Care 2020;43:597–606 | <https://doi.org/10.2337/dc19-1922>

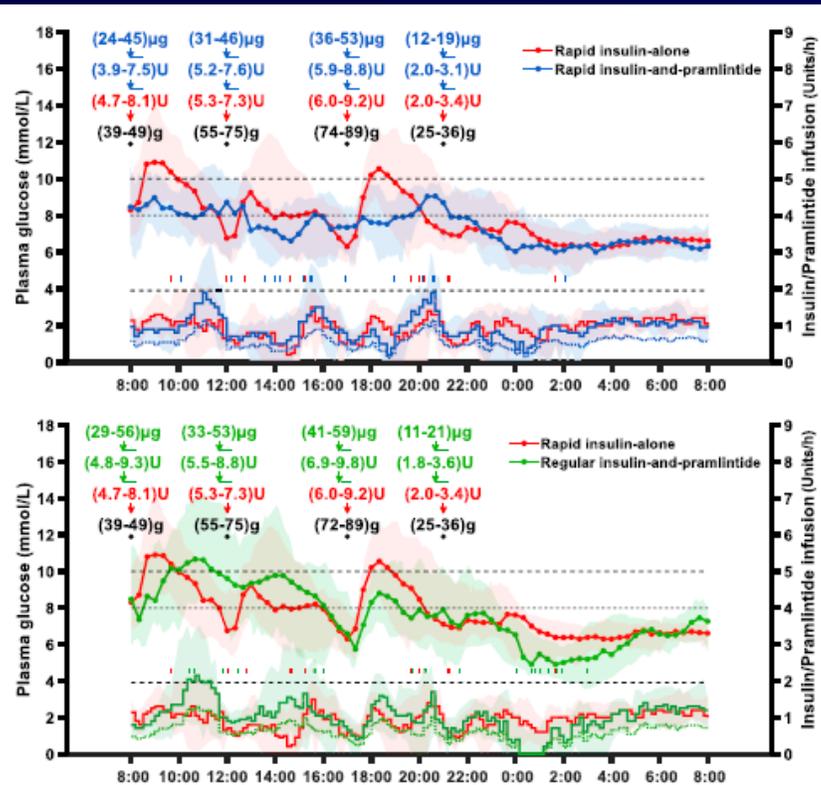


Figure 1—The median (IQR) profiles of glucose levels and hormonal deliveries during artificial pancreas visits. Meal and hormonal bolus values are (IQR). Hormonal boluses were composed of immediate and extended components on the dual-hormone visits. Small vertical lines indicate hypoglycemia events. Solid lines indicate glucose levels and basal insulin. Dotted lines indicate basal pramlintide. Note that the shaded IQR areas indicate the upper and lower 25% of participants. For example, the figure shows that during the insulin-alone visits, 25% of the participants had glucose levels >14 mmol/L after breakfast.

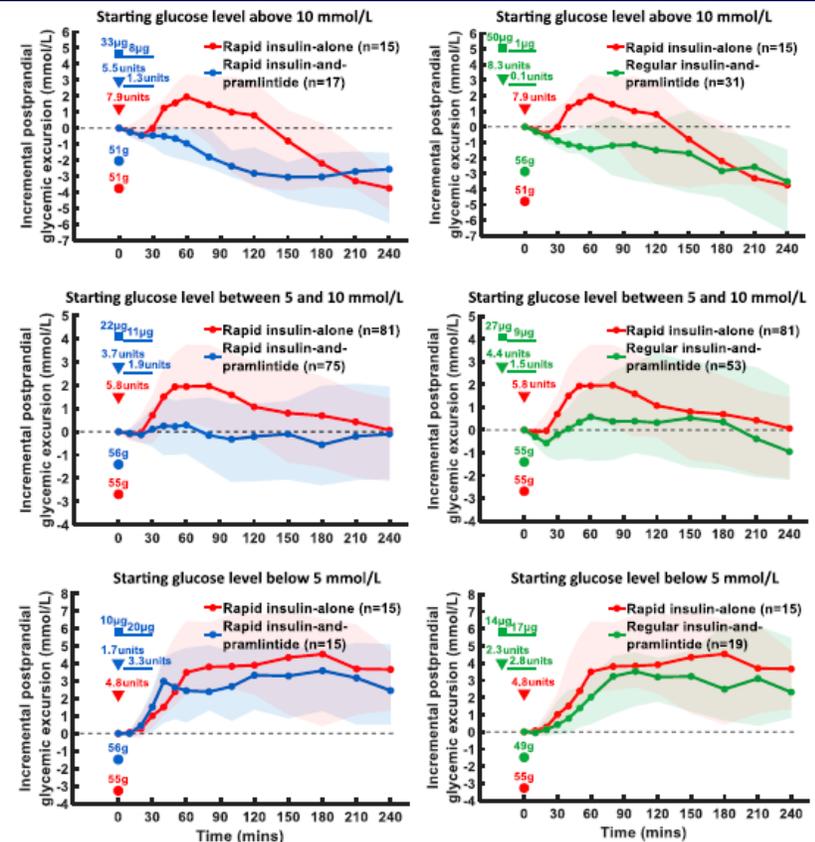


Figure 2—Median (IQR) postprandial glucose levels during artificial pancreas visits. During rapid insulin-and-pramlintide visits, insulin and pramlintide boluses had mean 81% immediate component when premeal glucose levels were >10 mmol/L, 66% immediate component when premeal glucose levels were between 5 and 10 mmol/L, and 34% immediate component when premeal glucose levels were <5 mmol/L. During regular insulin-and-pramlintide visits, the immediate components were 99%, 75%, and 45%, respectively.

Advanced Closed-Loop Control System Improves Postprandial Glycemic Control Compared With a Hybrid Closed-Loop System Following Unannounced Meal

Diabetes Care 2021;44:2379–2387 | <https://doi.org/10.2337/dc21-0932>

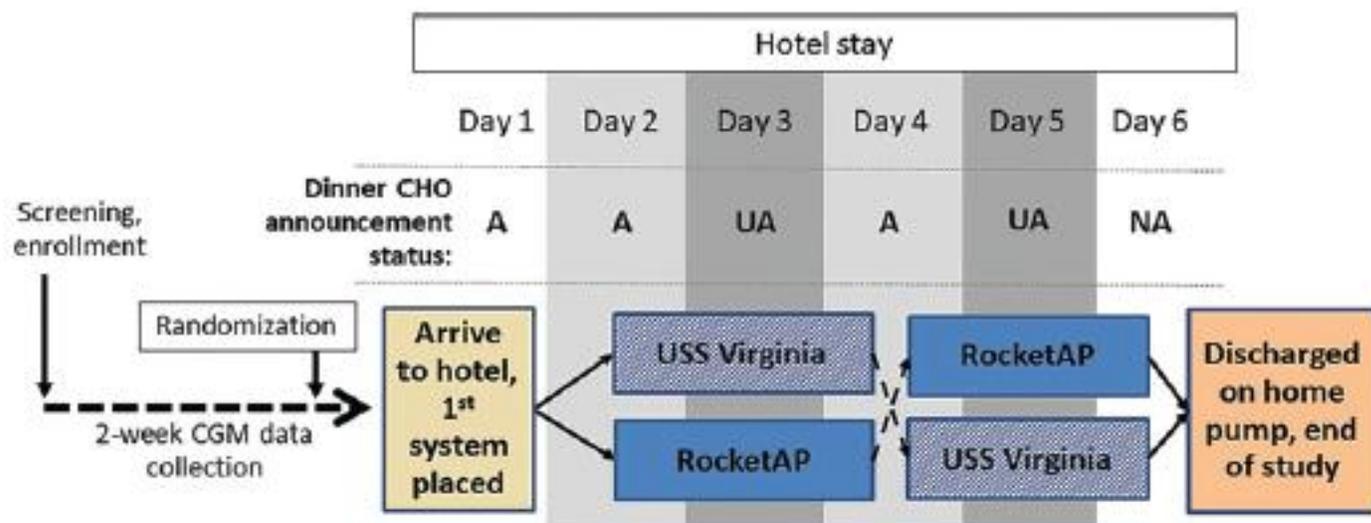


Figure 1—Study design. During the 5-night study, participants were randomly assigned to start the study on either the USS Virginia or RocketAP system, which were then switched on day 4. Four 23-h periods were compared, with each system being tested for glycemic performance following when the dinner carbohydrate (CHO) content was announced (A) or unannounced (UA). On the final day of the study, participants were discharged to home before lunch, thus the carbohydrate announcement was not applicable (NA).

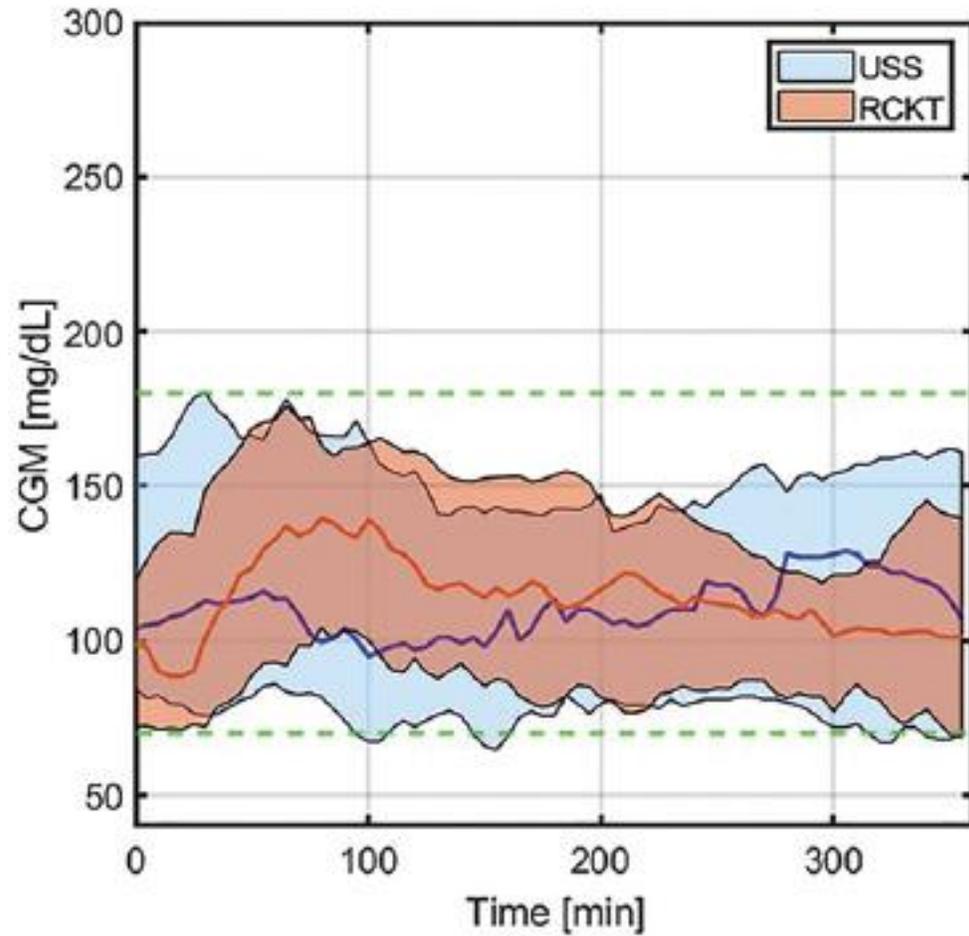
The BPS system runs every 5 min by estimating the probability that a meal-like disturbance has occurred in the prior 30 min. A priming bolus will then be requested when the disturbance probability is greater than a specific set of thresholds: for $P = 0.3, 0.5, 0.7,$ and 0.9 , the bolus requests will be of 3%, 5%, 6%, and 7% of total daily insulin, respectively. Every new dose will account for the insulin-on-board from preceding BPS doses.

Table 1—Glycemic outcomes during unannounced and announced dinners, 6:00 P.M.–12:00 A.M.

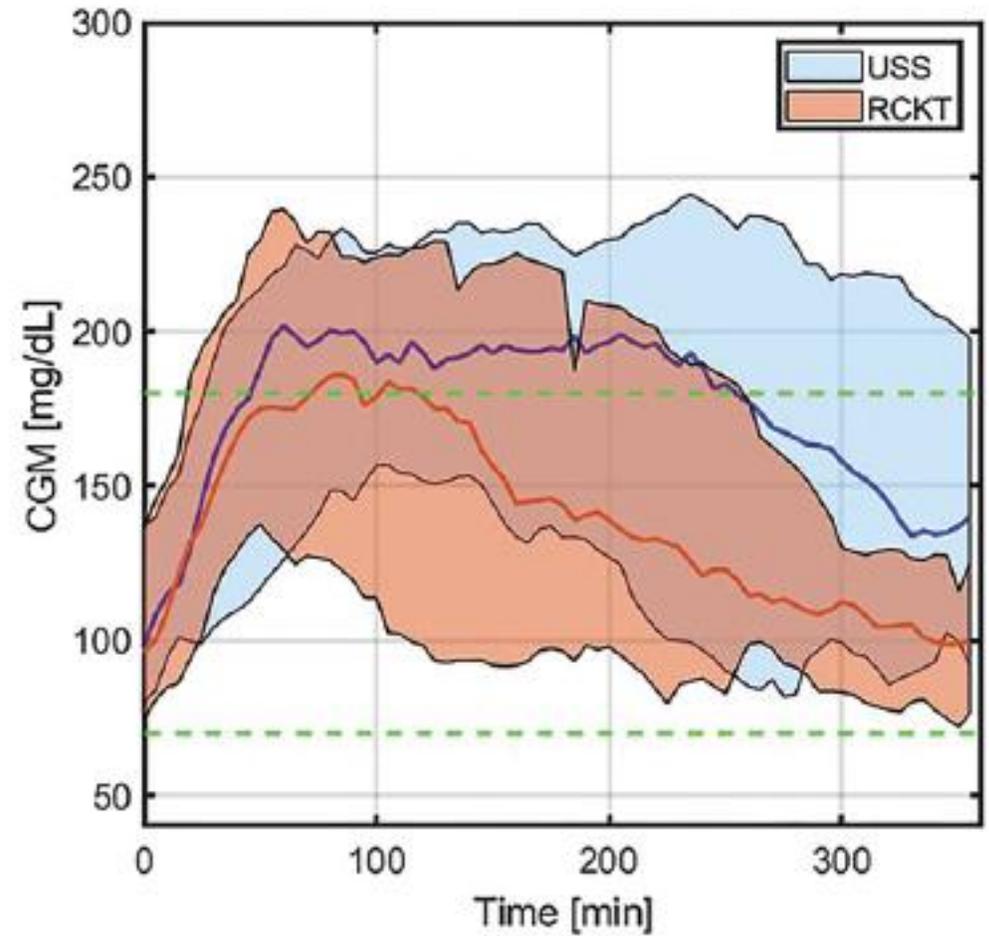
	Unannounced dinner (primary outcome)			Announced dinner (secondary outcome)		
	USS	RCKT	<i>P</i> value	USS	RCKT	<i>P</i> value
Glycemic metrics						
CGM glucose (mg/dL)	166 ± 26	141 ± 21	0.001^a	114 ± 26	114 ± 11	0.45
Percentage of CGM time						
<50 mg/dL (<2.8 mmol/L)	0 (0–0)	0 (0–0)	1	0 (0–0)	0 (0–0)	1
<60 mg/dL (<3.3 mmol/L)	0 (0–0)	0 (0–0)	0.5	0 (0–0)	0 (0–0)	0.08
<70 mg/dL (<3.9 mmol/L)	0 (0–0)	0 (0–1)	0.2	0.7 (0–8)	0 (0–0)	0.04^b
70–140 mg/dL (3.9–7.8 mmol/L)	27 (22–36)	49 (41–59)	0.002^b	82 (57–89)	86 (69–94)	0.13
70–180 mg/dL (3.9–10.0 mmol/L)	53 (40–71)	83 (64–93)	0.004^b	93 (85–99)	100 (99–100)	0.004^b
>180 mg/dL (>10.0 mmol/L)	47 (28–60)	17 (1.3–34)	0.01^b	0 (0–1)	0 (0–0)	0.10
>250 mg/dL (>13.9 mmol/L)	0 (0–0)	0 (0–0)	1	0 (0–0)	0 (0–0)	1
>300 mg/dL (>16.7 mmol/L)	0 (0–0)	0 (0–0)	1	0 (0–0)	0 (0–0)	1
CGM SD (mg/dL)	40 ± 13	37 ± 17	0.2	20 ± 8.5	23 ± 7	0.11
CGM coefficient of variation (%)	24 ± 9	26 ± 9	0.4	17.5 ± 7.1	20 ± 6	0.10
Safety metrics						
Severe hypoglycemia (<i>n</i> events)	0 (0–0)	0 (0–0)	1 ^b	0 (0–0)	0 (0–0)	1 ^b
Diabetes ketoacidosis (<i>n</i> events)	0 (0–0)	0 (0–0)	1 ^b	0 (0–0)	0 (0–0)	1 ^b
Technical performance metrics						
Time in CLC (%)	95 ± 15	100 ± 1	0.16	92 ± 17	99 ± 2	0.16
Total injected insulin (IU)	14 ± 4	15 ± 5	0.21	14 ± 4	15 ± 7	0.22

Data are presented as mean ± SD or median (IQR). Significance levels <0.05 are presented in bold. ^aOne-sided paired *t* test. ^bWilcoxon signed rank test.

A Announced dinner: RCKT vs. USS



B Unannounced dinner: RCKT vs. USS



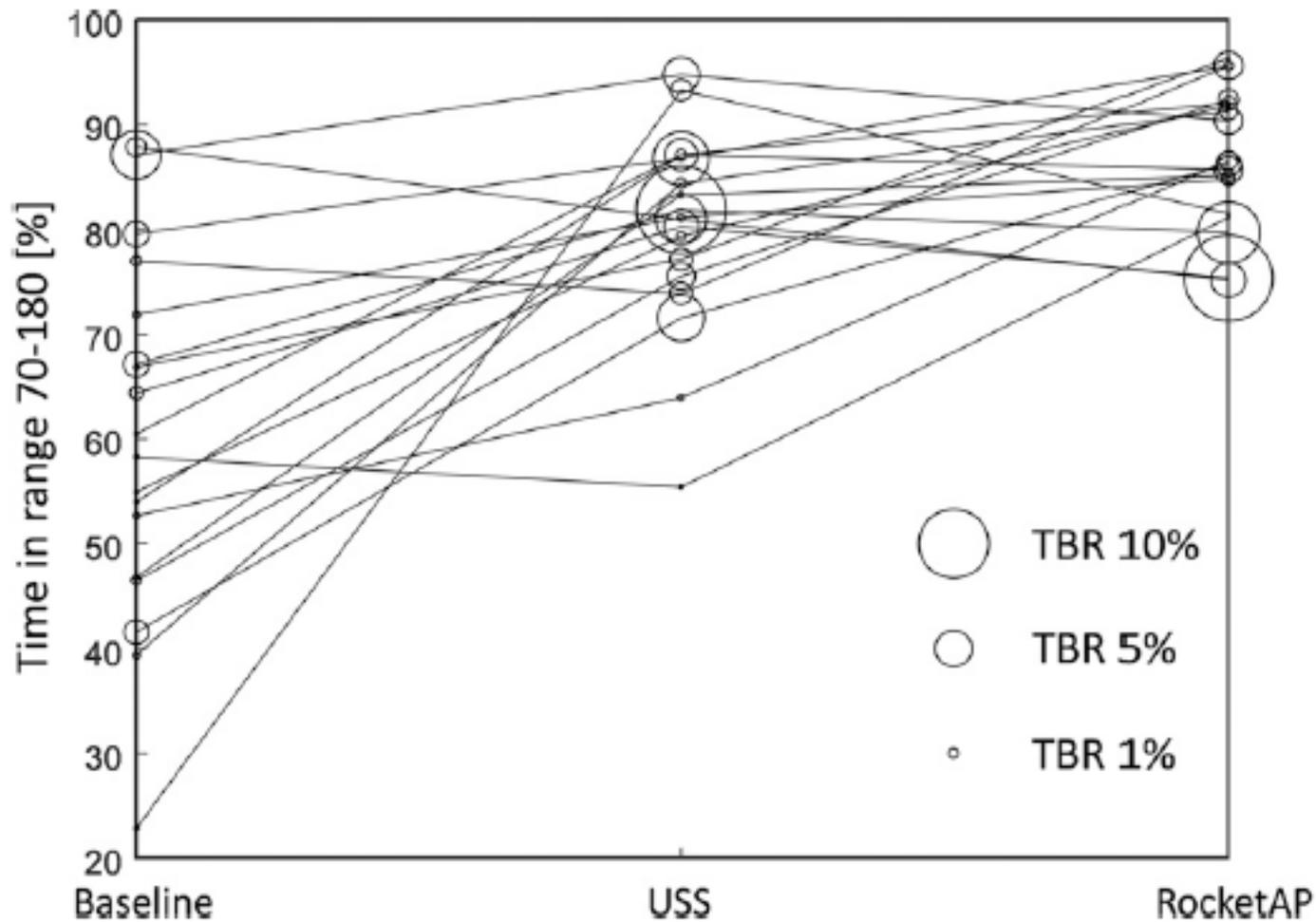


Figure 3—Comparison of TIR at baseline and on each CLC system. Each set of points connected between baseline, USS Virginia, and RocketAP represents an individual participant’s TIR at that point. The size of the circle represents the percentage of time <70 mg/dL during the entire period on that system. TBR, time below range.

In conclusion, this system, with automatic prandial bolus priming, achieved 83% in the 6-h period around a dinner without carbohydrate announcement among adolescents. While HCL overcomes some of the inherent delays in CLC via calculating insulin needed for carbohydrate and delivering the dose before eating, automated meal detection for prandial glycemic management may help achieve an acceptable degree of control for individuals who miss opportunities to announce carbohydrate ingestion during use of a CLC system.

Evaluation of an Automated Priming Bolus for Improving Prandial Glucose Control in Full Closed Loop Delivery

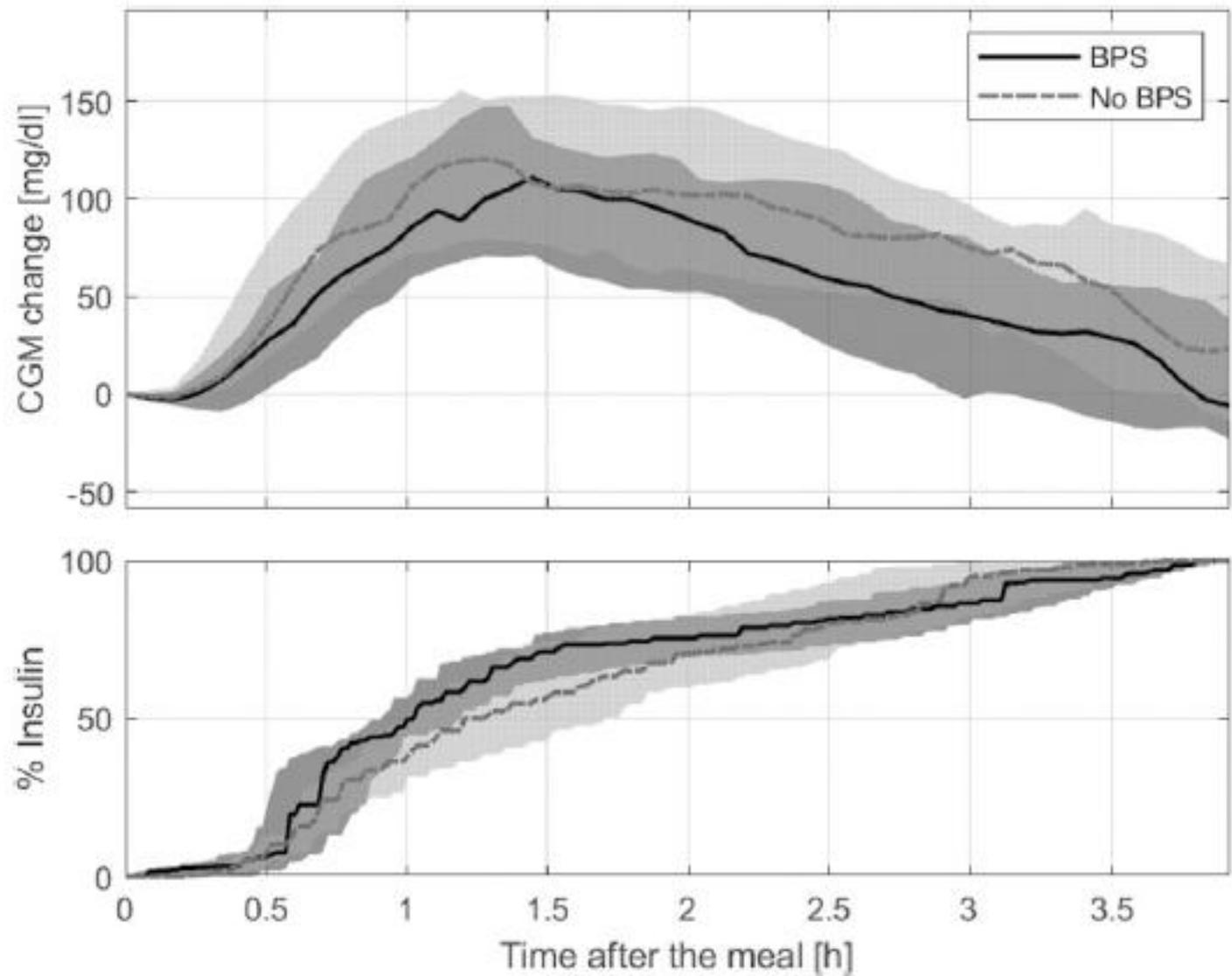
TABLE 2. GLYCEMIC OUTCOMES FOR DAYTIME (6 AM–2 AM), OVERNIGHT (12 AM–6 AM) PERIODS, AND OVERALL (12 PM–12 PM)

	Daytime		Overnight		Overall	
	No BPS	BPS	No BPS	BPS	No BPS	BPS
Mean BG	153 [144.2, 165.3]	152.3 [133.3, 171] ^a	117.7 [109.3, 119]	113.3 [111.1, 115.2]	146.6 [132.2, 151.7]	145.9 [128.4, 155.9] ^a
% time [70–180] mg/dL	65.7 [58.6, 80.6] ^a	70.6 [62.2, 76.5]	100 [100, 100]	100 [100, 100]	74.3 [68.9, 85.6] ^a	75.4 [70.8, 82.4]
% time [70–140] mg/dL	44.4 [33, 60.2] ^a	52.3 [41.2, 57.8] ^a	100 [83.7, 100]	93.1 [87.5, 100]	58.3 [49.1, 67.4]	61.1 [50.8, 68] ^a
% time <70 mg/dL	0 [0, 1.3]	0 [0, 2.1]	0 [0, 0]	0 [0, 0]	0 [0, 1]	0 [0, 1.6]
% time <54 mg/dL	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]	0 [0, 0]
% time >180 mg/dL	34.3 [18.3, 37.8]	25.9 [19.8, 37.5] ^a	0 [0, 0]	0 [0, 0]	25.7 [14.4, 28.4]	19.4 [14.8, 28.1]
% time >250 mg/dL	6 [3.2, 15.6]	9.7 [2, 15.3] ^a	0 [0, 0]	0 [0, 0]	4.2 [2.3, 11.7]	7.3 [1.4, 11.8] ^a
% CV-glucose	35.6 [29.4, 37.5] ^a	38.5 [28.9, 46] ^a	19.1 [12.1, 10] ^a	14.8 [9.1, 18.9]	33.8 [30.5, 38.6] ^a	38.4 [29.4, 44.7] ^a
% SD-glucose (mg/dL)	52.2 [46.8, 60.9] ^a	59 [44.5, 70.6] ^a	14.5 [11, 23.5] ^a	15.1 [10.1, 21.1] ^a	48.9 [44, 58.9] ^a	54.2 [43.9, 65.5] ^a
HBGI	6.6 [4, 8]	6.5 [3.8, 9.8] ^a	0.4 [0.1, 0.7]	0.3 [0.1, 0.5]	5.1 [3.1, 6]	5 [2.9, 7.5] ^a
LBGI	0.4 [0, 0.7] ^a	0.6 [0.3, 0.8]	0.2 [0.1, 0.4]	0.2 [0.2, 0.8]	0.4 [0.1, 0.7]	0.5 [0.4, 0.6]
Hypoglycemia Events	0 [0, 1]	0 [0, 1]	0 [0, 0]	0 [0, 0]	0 [0, 1]	1 [0, 1.8]
Total Daily Insulin (U/kg)	0.4 [0.29, 0.45] ^a	0.4 [0.31, 0.47] ^a	0.07, [0.06, 0.09] ^a	0.08 [0.05, 0.09] ^a	0.47 [0.37, 0.52] ^a	0.45 [0.36, 0.55] ^a
Total Daily Basal Insulin (U/kg)	0.34 [0.26, 0.4] ^a	0.27 [0.24, 0.34] ^a	0.07, [0.06, 0.09] ^a	0.08 [0.05, 0.09] ^a	0.41 [0.35, 0.46] ^a	0.34 [0.3, 0.42] ^a

^aOutcome is normally distributed. Data are presented as median [25th, 75th] percentiles.

BPS, bolus priming system; BG, blood glucose; LBGI, low blood glucose index; HBGI, high blood glucose index.

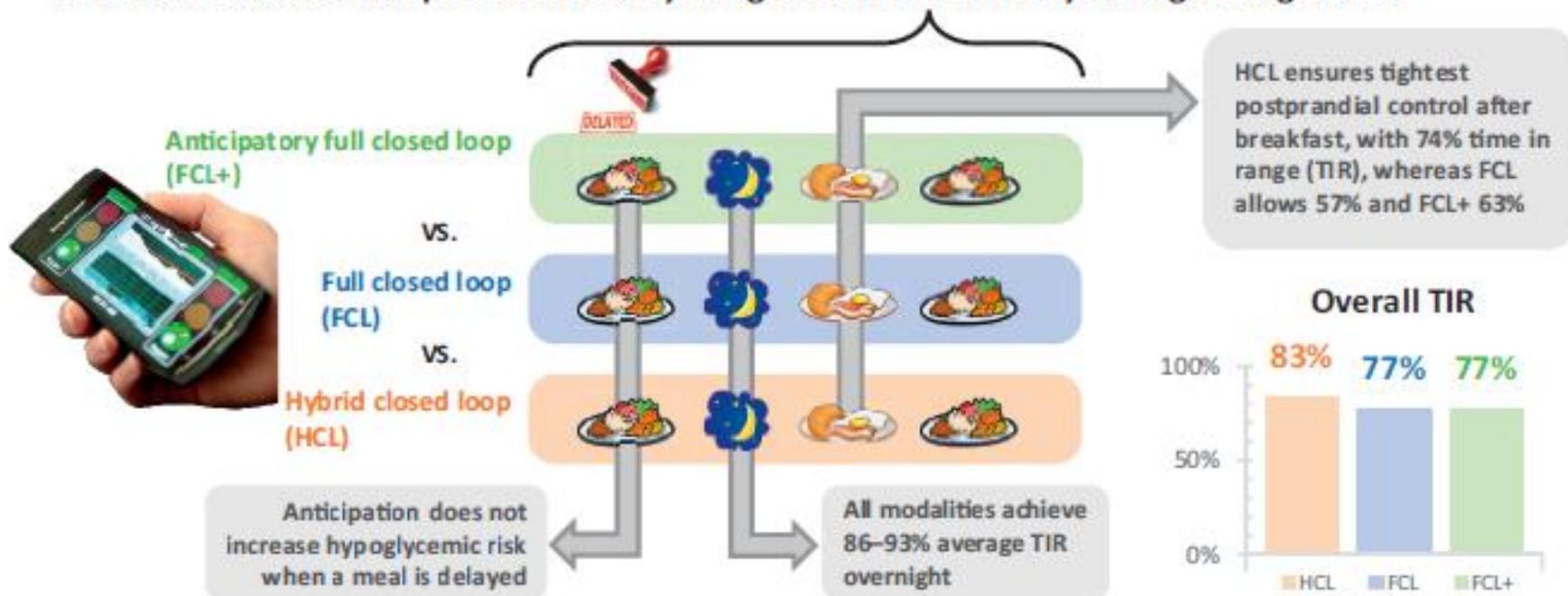
FIG. 1. Change in glucose levels over time after a meal for the automated insulin delivery (AID) system with (solid black line) and without (dashed-dotted gray line) bolus priming system (BPS) engaged. Lines represent the median values. Dark and light shaded areas represent 25th–75th percentile ranges.



Assessment of Meal Anticipation for Improving Fully Automated Insulin Delivery in Adults With Type 1 Diabetes

Diabetes Care 2023;46(9):1652–1658

N = 35 adults with type 1 diabetes completed three randomized 24-h hotel admissions testing three modalities of closed-loop insulin delivery using the latest University of Virginia algorithm



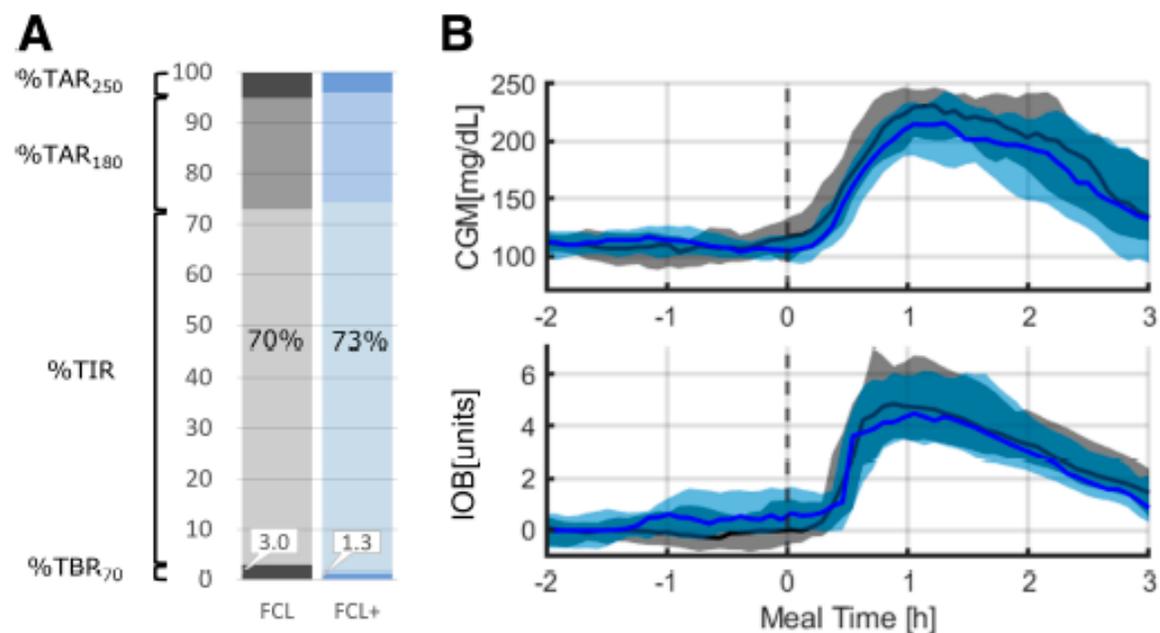


Figure 2—Glucose levels over time by AID system, FCL+ (blue) and FCL (gray), for the time window from 2 h before breakfast to 3 h after breakfast. **A**: Percent time <70 (TBR₇₀), TIR, time >180 (TAR₁₈₀), and time >250 mg/dL (TAR₂₅₀). **B**: CGM and IOB data shown centered over the meal. Black vertical dotted line represents commencement of the meal. Solid blue and black lines and shaded areas represent mean glucose and 25th–75th percentiles, respectively.

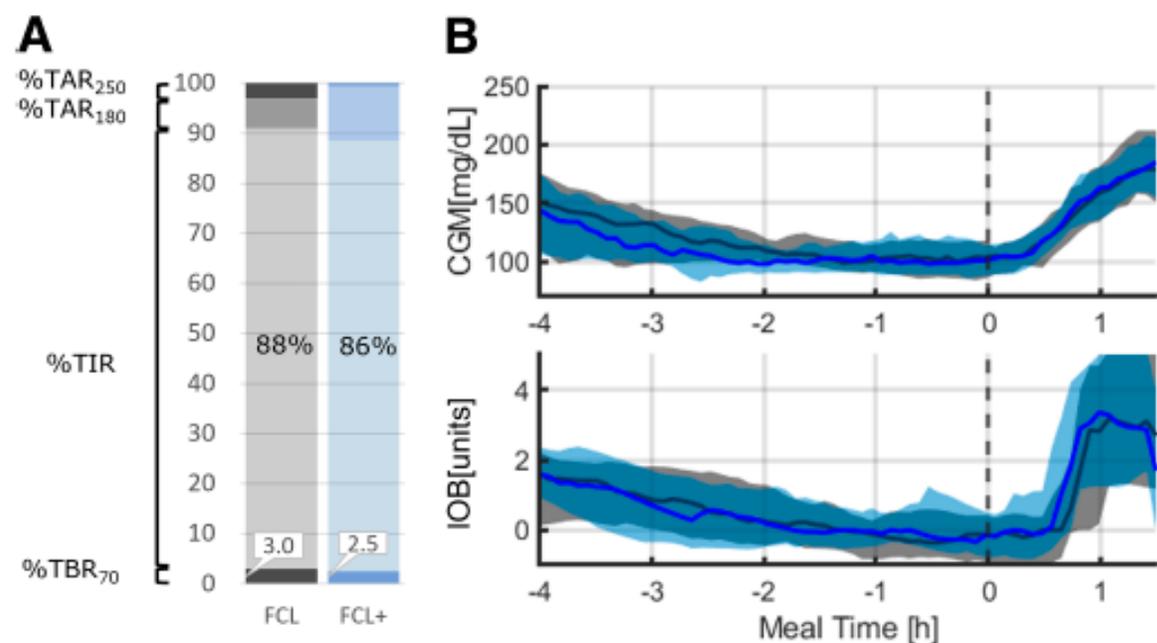


Figure 3—Glucose levels over time by AID system, FCL+ (blue) and FCL (gray), for the time window from 4 h before dinner to 1.5 h after dinner. **A**: Percent time <70 (TBR₇₀), time-in-range (TIR), time >180 (TAR₁₈₀), and time >250 (TAR₂₅₀). **B**: CGM and IOB data shown centered over the meal. Black vertical dotted line represents commencement of the meal. Solid blue and black lines and shaded areas represent mean glucose and 25th–75th percentiles, respectively.

Miniaturized Neural Networks for Deploying Fully Closed Loop Insulin Delivery Systems: A Pilot Study Featuring Flexible Meal Announcement Options

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Chaitanya L. K. Koravi, MS¹, Anas El Fathi, PhD¹ , Sue A. Brown, MD¹,
Mark D. DeBoer, MD¹, and Marc D. Breton, PhD¹ 

Journal of Diabetes Science and Technology

DOI: 10.1177/19322968251364283

Methods: In a randomized crossover trial, six adults with type 1 diabetes completed seven days of usual care and seven days using AIDANET in free-living conditions. AIDANET is designed to enable FCL control, but carbohydrate counting and a novel easy-bolus strategy were enabled for one day each to test the system in hybrid closed loop modalities.

Study AID System

This work uses the UVA-AIDANET system as the AID system which has been described in previous works.^{10,11,21,22} The UVA-AIDANET system has four main components: the NN which modulates basal delivery every 5 minutes; a Bolus Priming System (BPS) which automatically provides an initial bolus for meal-like disturbances;²¹ a hyperglycemia mitigation system which provides correction boluses for sustained hyperglycemia; and a performance-based adaptation system which modulates overall system aggressiveness based on glycemic metrics.²⁵ The system was designed to primarily operate without user meal announcements.

Table 1. Baseline Characteristics of Participants.

A1c (%)	7.17 ± 0.41	
Age (y)	40.3 ± 7.7	
Weight (kg)	83.4 ± 14.6	
BMI (kg/m ²)	29.7 ± 3.9	
Diabetes duration (y)	24.9 ± 8.7	
Gender	Female	3
	Male	3
Ethnicity	Not Hispanic or Latino	6
Race	White	6
CGM use	Dexcom G6	3
	Dexcom G7	3
Pump use	Tandem / t: slim X2 with Control-IQ	4
	Insulet / Omnipod 5	2

Values are Presented as: Mean ± Standard Deviation, or Count (#).

Table 2. Glycemic Metrics of AIDANET Compared to Usual Care.

	Usual care	AIDANET	Difference	FCL Days	Difference
Mean CGM	168.0 ± 24.3	161.3 ± 16.7	-6.7 [-26.45, 13.05]	158.5 ± 18.0	-9.5[-32.61, 13.61]
GMI	7.3 ± 0.6	7.2 ± 0.4	-0.2 [-0.63, 0.31]	7.1 ± 0.4	-0.2 [-0.78, 0.33]
Time in range	63.9 ± 14.9	66.4 ± 8.3	2.5 [-8.29, 13.34]	67.7 ± 9.4	3.8 [-10.12, 17.77]
Time in tight range	38.5 ± 13.8	42.7 ± 10.8	4.1 [-8.32, 16.62]	43.3 ± 11.6	4.8 [-8.14, 17.66]
Time below 70	0.9 ± 1.0	1.6 ± 1.8	0.7 [-1.67, 3.07]	1.8 ± 2.0	0.9 [-1.59, 3.45]
Time below 54	0.1 ± 0.2	0.3 ± 0.6	0.2 [-0.46, 0.85]	0.3 ± 0.6	0.2 [-0.48, 0.86]
Time above 180	35.2 ± 15.2	32.0 ± 8.8	-3.2 [-13.78, 7.33]	30.5 ± 9.8	-4.8 [-18.31, 8.79]
Time above 250	10.3 ± 8.9	9.7 ± 6.3	-0.6 [-8.15, 6.86]	8.2 ± 8.0	-2.2 [-12.26, 7.96]
Coefficient of variation	34.3 ± 3.8	36.0 ± 3.0	1.7 [-3.67, 7.09]	34.7 ± 4.3	0.4 [-5.91, 6.74]
Standard deviation	57.9 ± 11.8	58.0 ± 6.8	0.1 [-0.34, 0.60]	55.1 ± 8.4	-2.8[-3.33,-2.22]
Total Daily Insulin	66.2 ± 26.5	75.3 ± 33.1	9.1 [-4.10, 22.28]	69.3 ± 29.1	3.1 [-8.20, 14.35]

Values are shown as: mean ± standard deviation, or mean [95% CI].

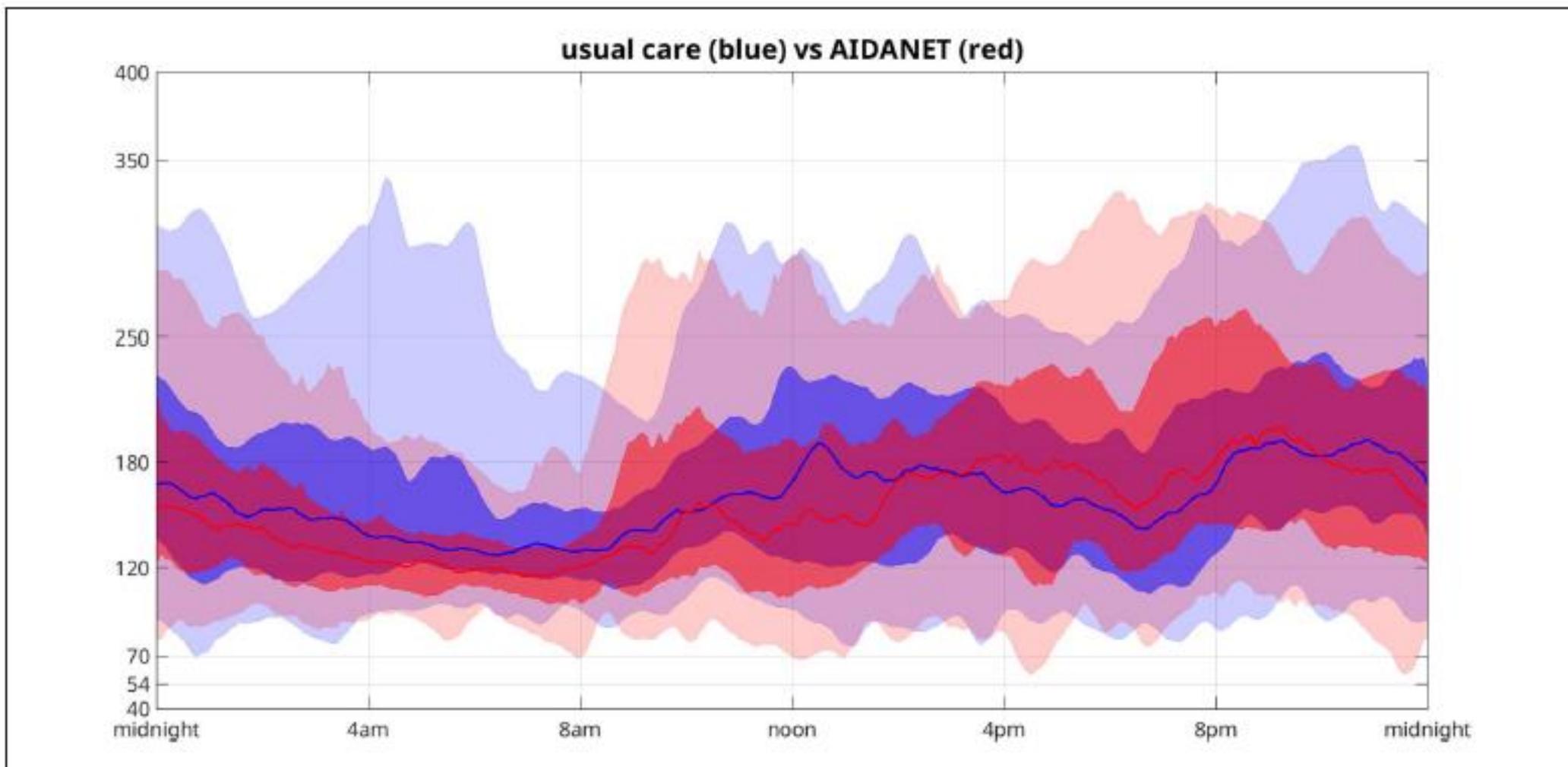


Figure I. Ambulatory glucose profile (AGP) plot of AIDANET vs usual care. Red shows AIDANET system and blue shows usual care period.

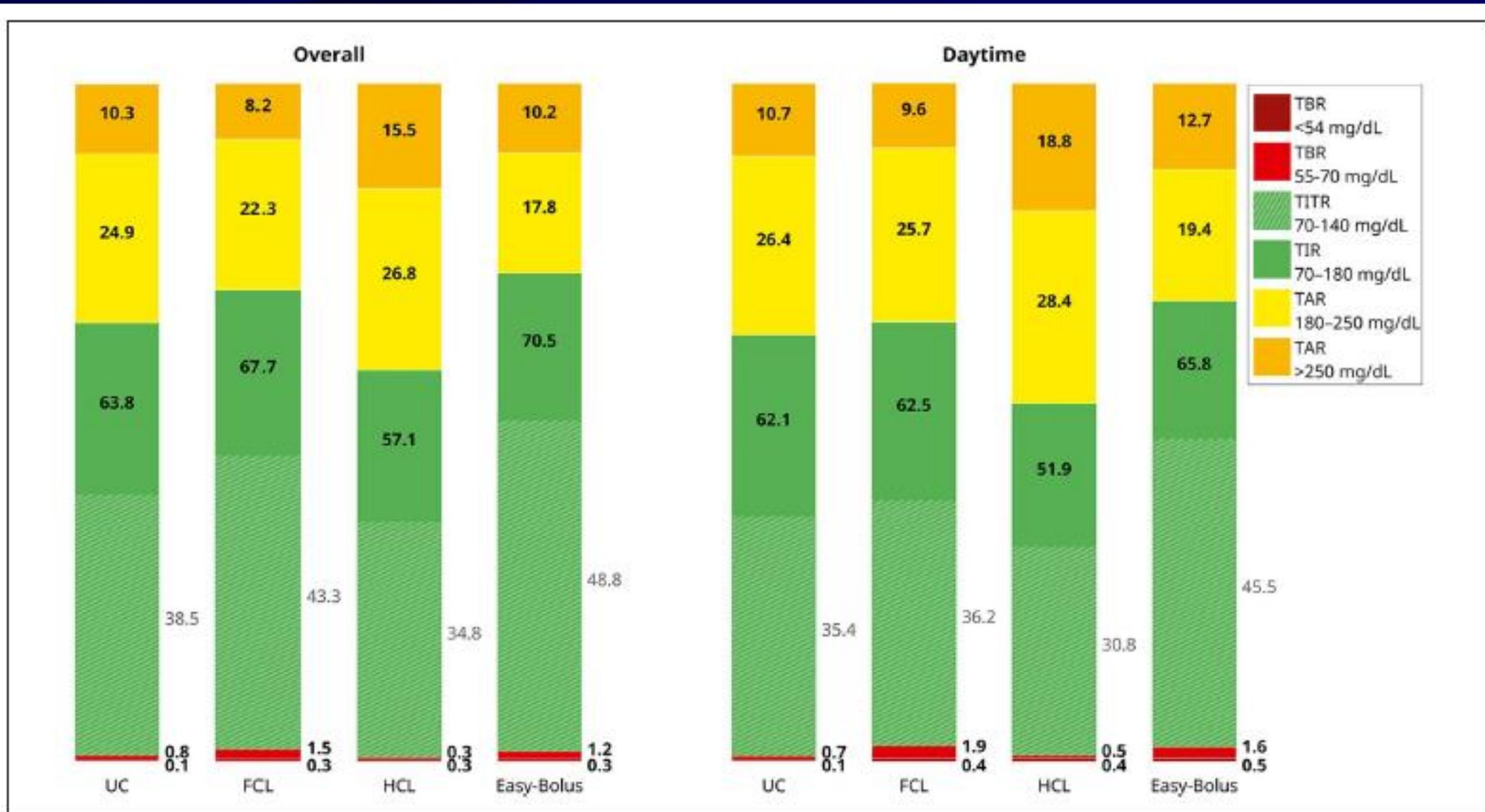


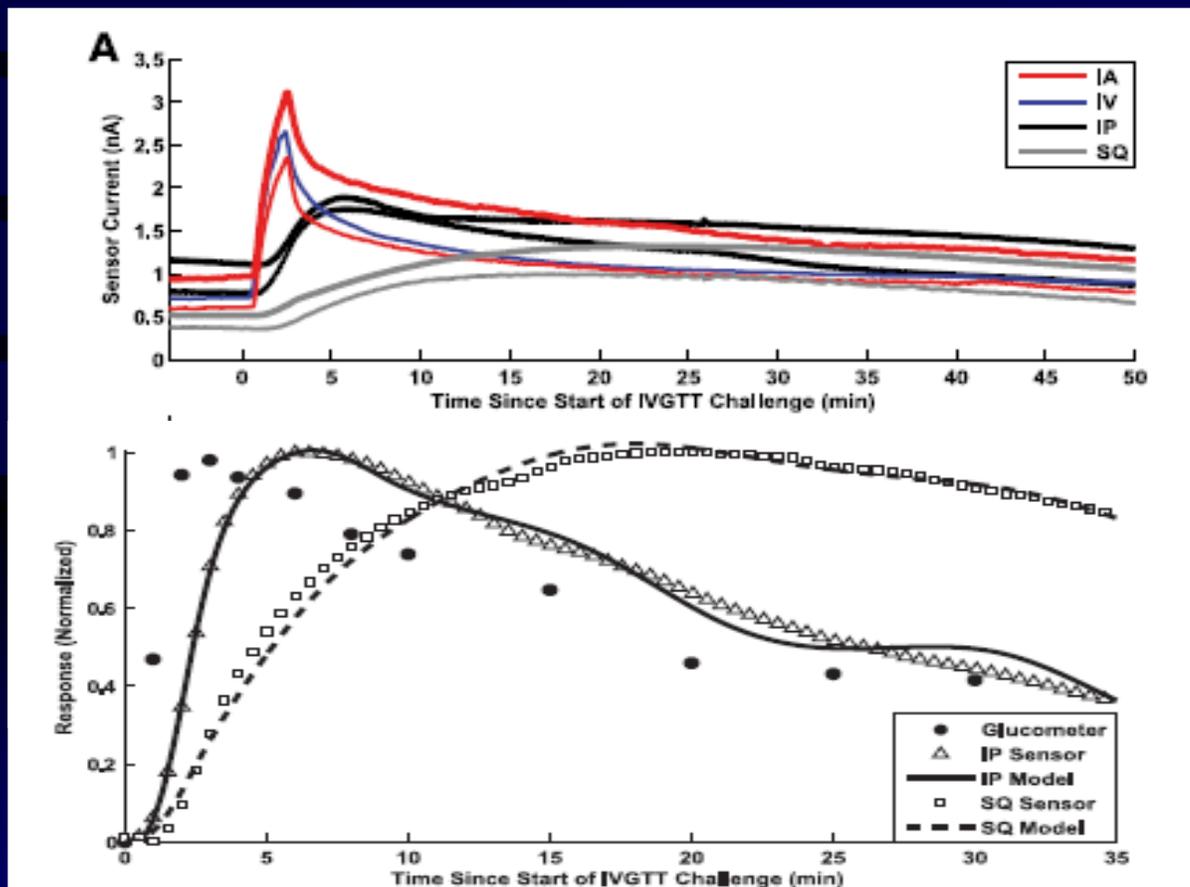
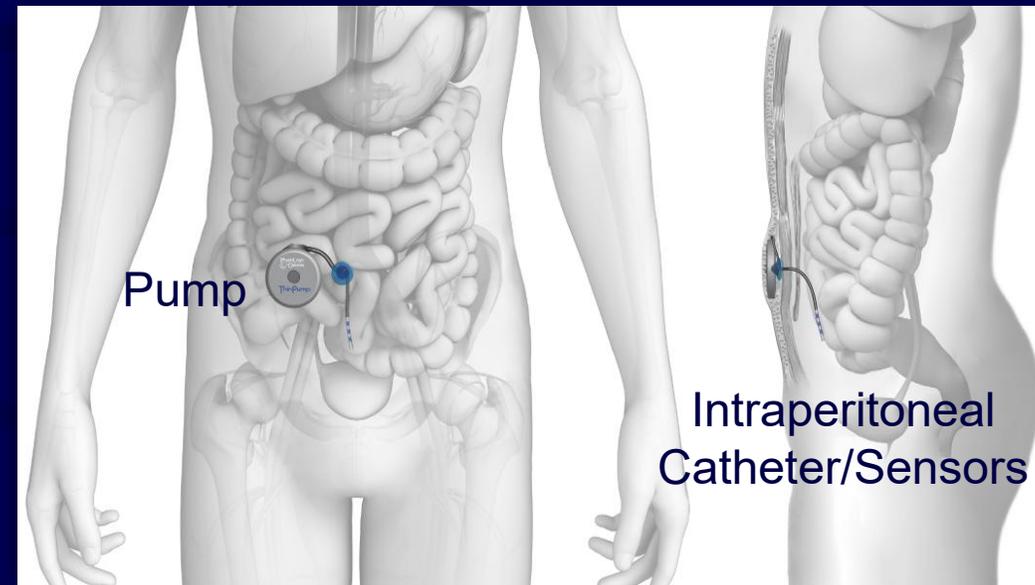
Figure 2. Ambulatory glucose report. Show the mean time in specified ranges of the system when using different bolus strategies. Results show overall (left) and daytime (6:00 AM to midnight) (right) periods.

Projets d'Amélioration de l'Insulinothérapie Automatisée

- Accélérer l'action de l'insuline
- Synchroniser les variations glycémiques et l'action de l'insuline
- **Accélérer la captation des variations glycémiques et l'action de l'insuline**
- Combiner les améliorations vers un système plus physiologique

Glucose Sensing in the Peritoneal Space Offers Faster Kinetics Than Sensing in the Subcutaneous Space

Diabetes 2014;63:2498–2505 | DOI: 10.2337/db13-1649



Three GOX Sensors on the IP Catheter

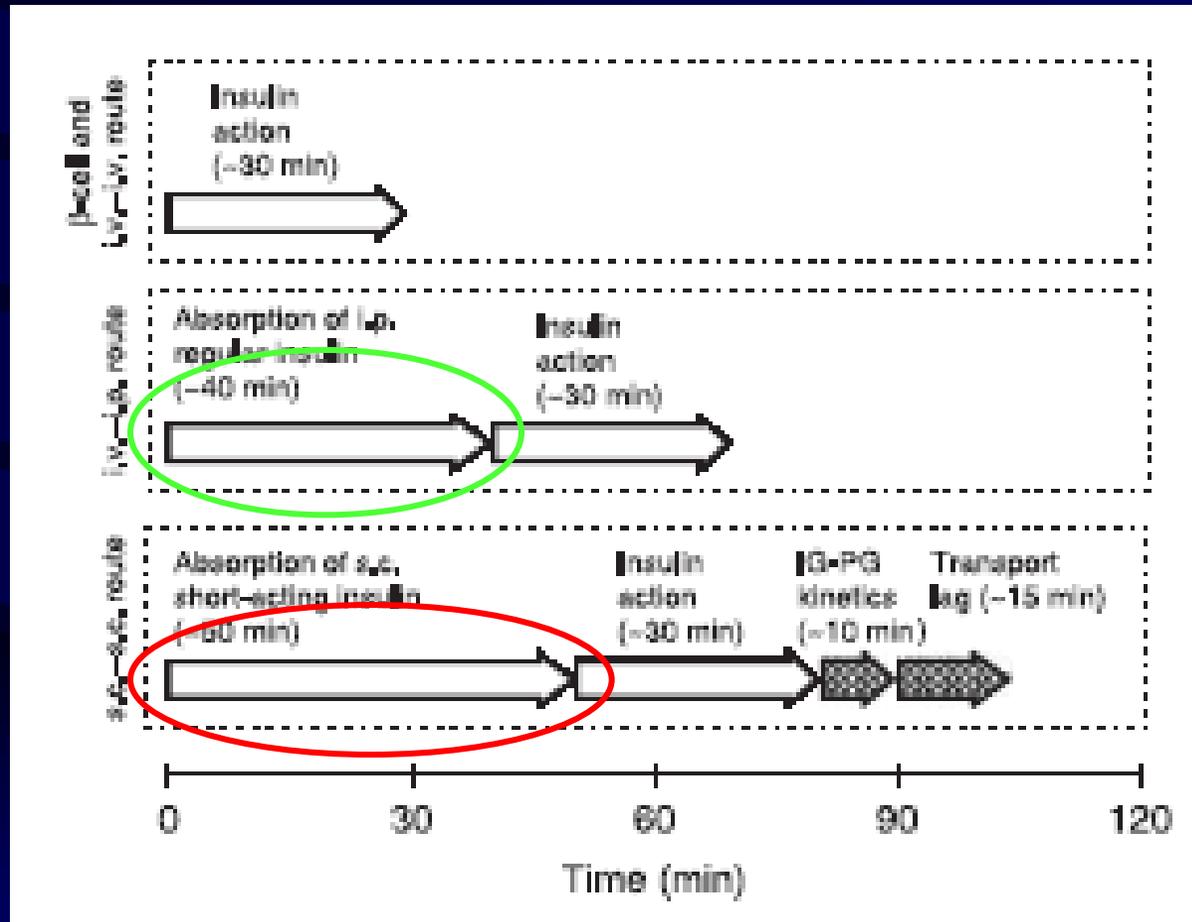


Insulin Action according to Infusion Route

IV

IP

SC



In silico design and validation of a time-varying PID controller for an artificial pancreas with intraperitoneal insulin delivery and glucose sensing F

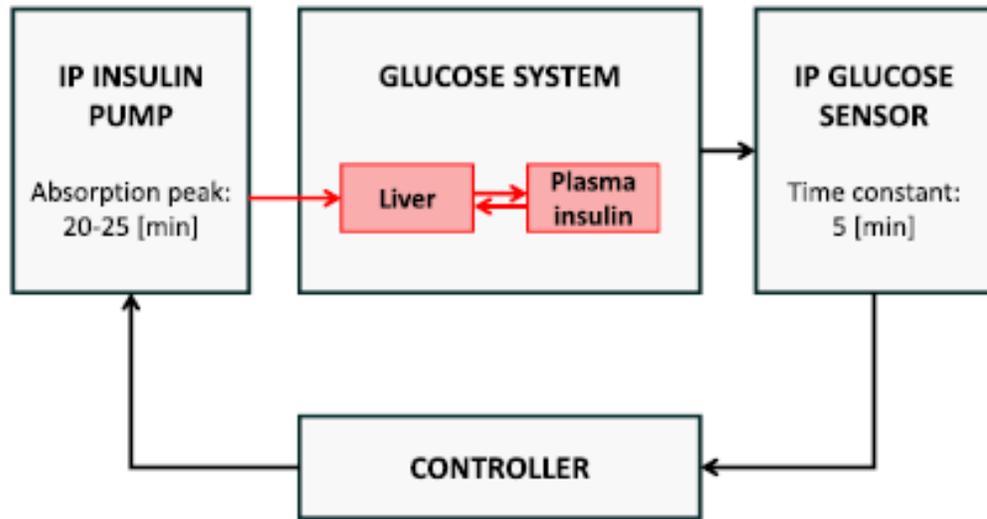


FIG. 6. Schematic representation of the IP-IP AP simulator. The insulin subsystem is evidenced in red.

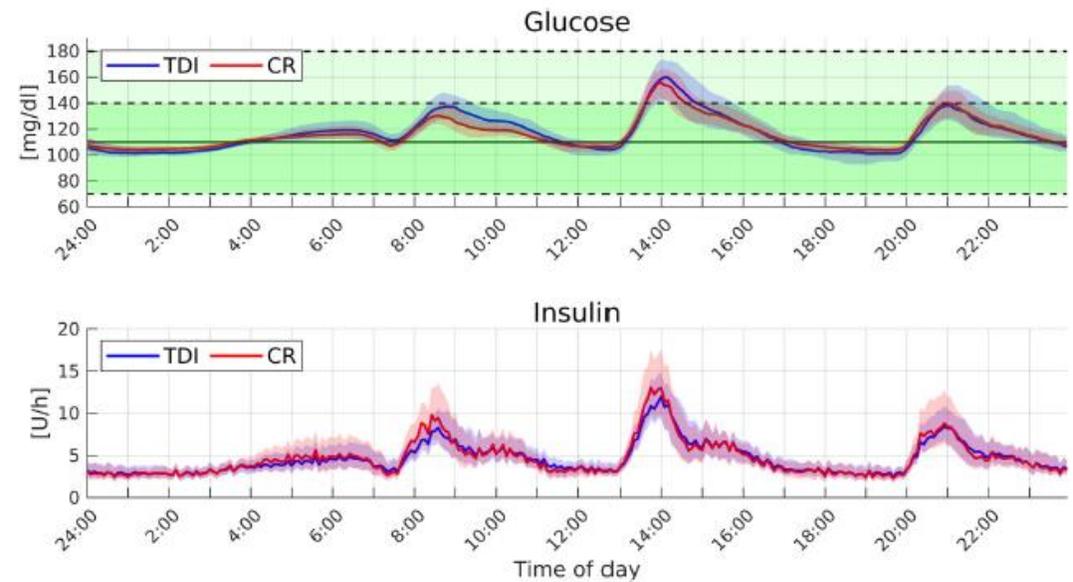


FIG. 5. Average time evolution of the glucose and insulin (median and confidence intervals) obtained with the PID controller based on TDI and CR personalizations in the robust setup.

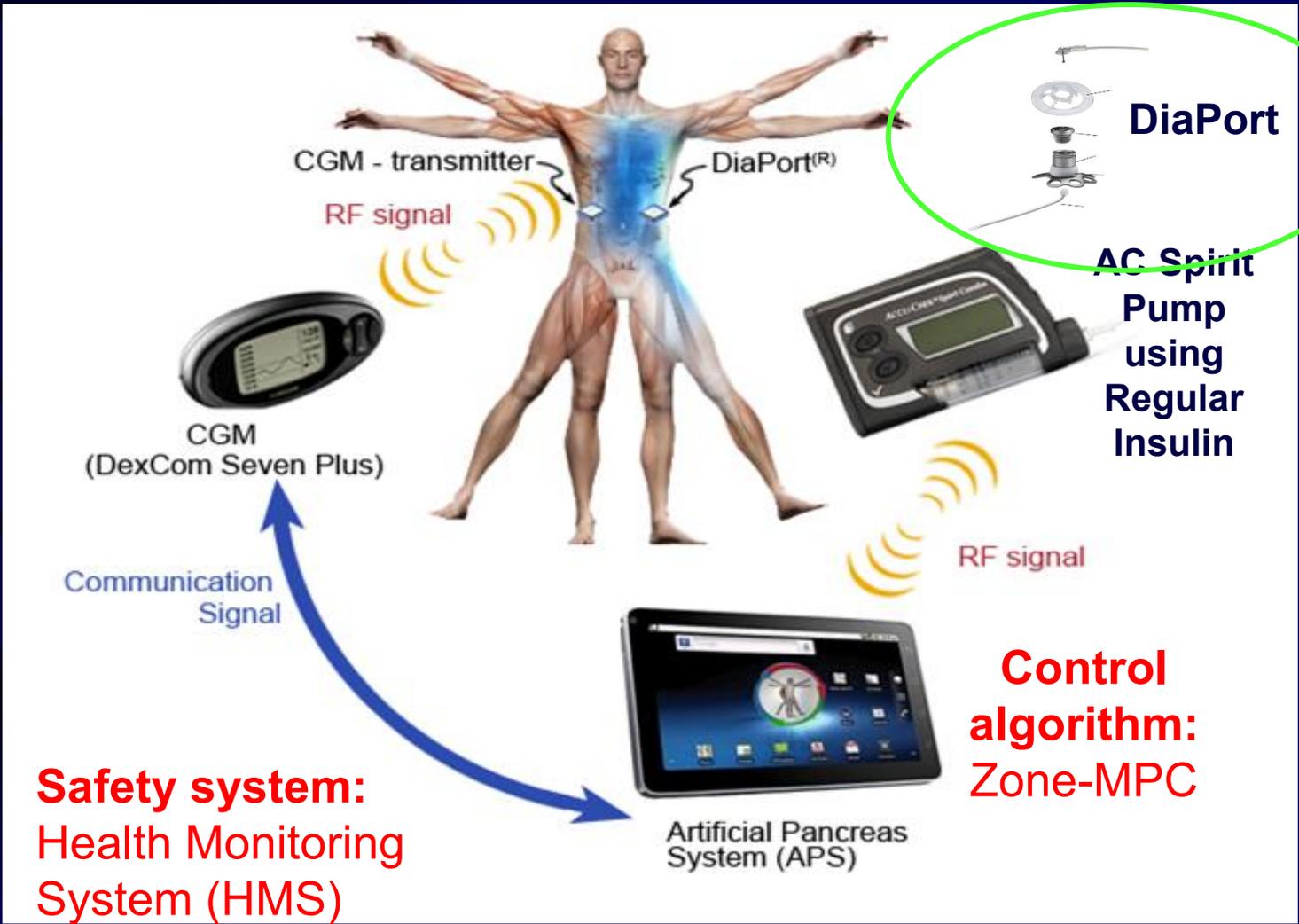
La diffusion portale rapide de l'insuline par voie IP permet d'opter pour un algorithme PID bi-compartmental.

Validation *in silico* de l'algorithme PID personnalisé sans annonce des repas

Projets d'Amélioration de l'Insulinothérapie Automatisée

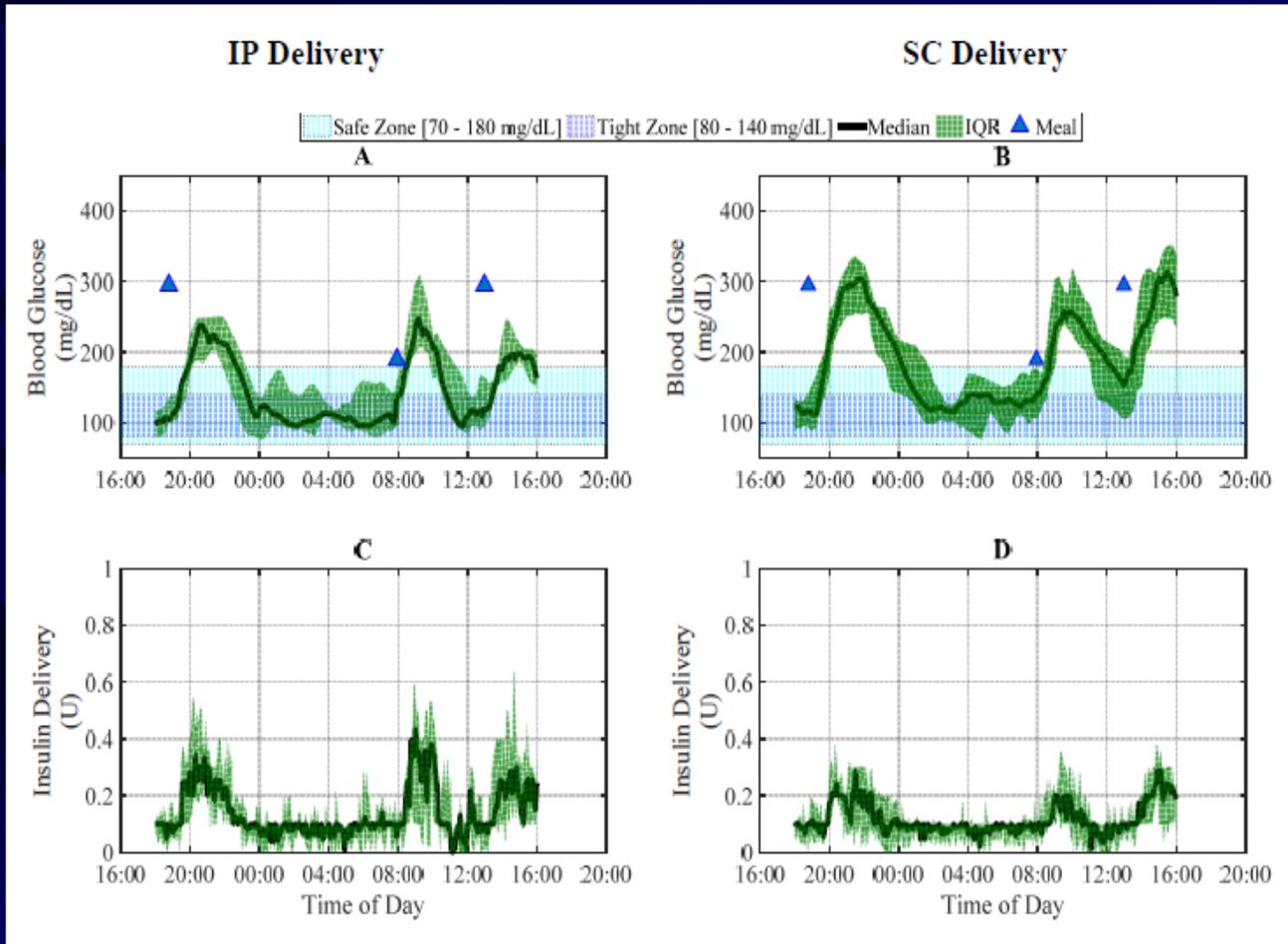
- Accélérer l'action de l'insuline
- Synchroniser les variations glycémiques et l'action de l'insuline
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- **Combiner les améliorations vers un système plus physiologique**

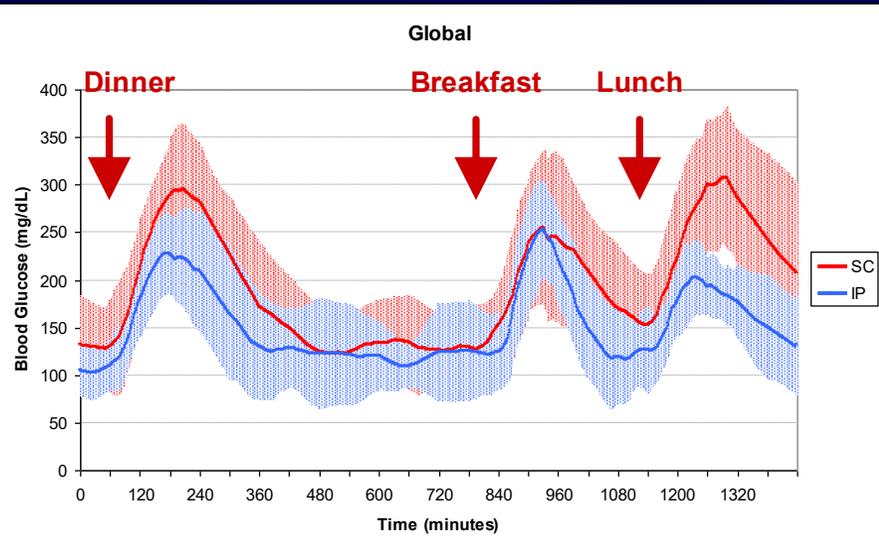
Artificial Pancreas with IP Insulin Infusion and SC Glucose Monitoring: A New Model to be Tested



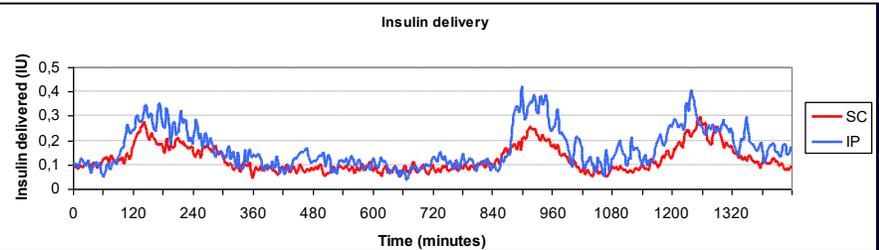


Intraperitoneal Insulin Delivery Provides Superior Glycemic Regulation to Subcutaneous Insulin Delivery in Model Predictive Control-based Fully-automated Artificial Pancreas in Patients with Type 1 Diabetes: A Pilot Study

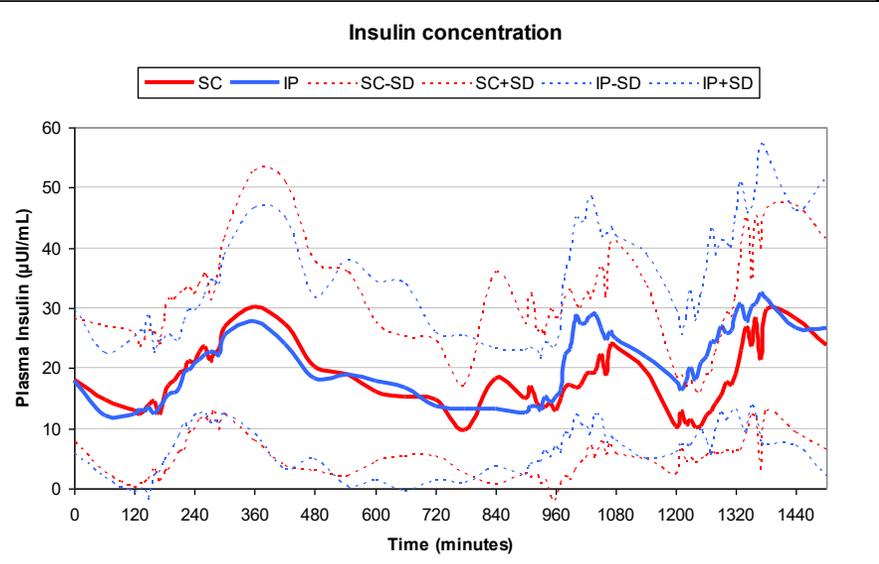




Mean blood glucose levels (mg/dl) were significantly lower with DiaPort use: **152 +/- 11** vs. **192 +/- 31** (p=0.004).



Significantly higher daily units of insulin were infused with IP route: **46 +/- 17** vs. **35 +/- 11** (p=0.006).



Similar plasma insulin levels with IP or SC route suggest hepatic extraction of insulin plays a role with IP infusion.

ThinPump™ | Smaller and Thinner



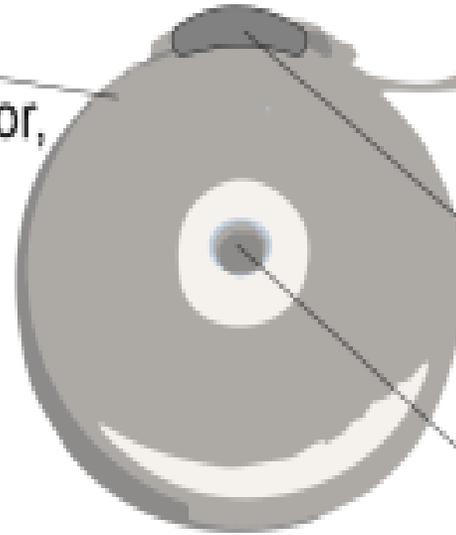
The ThinPump™ is **less than half** of the size of the Medtronic MIP.

ThinPump™ AP is Bluetooth enabled – upgrade to **closed-loop** with only a software upgrade
Re-implant is not required.

L'Objectif de MuSiC4Diabetes: une Cellule Bêta Digitale, Organe Artificiel Implantable

implant with:

- multiparameter sensor,
- MEMS pump,
- system control,
- algorithm,
- battery and
- insulin reservoir



physiologic delivery
in the peritoneal cavity

spectrometer, sensing
glucose, ketone and lactate

port for insulin refill

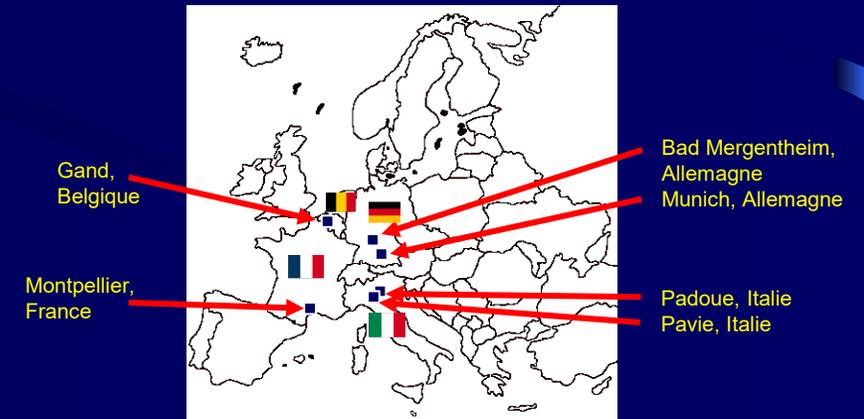
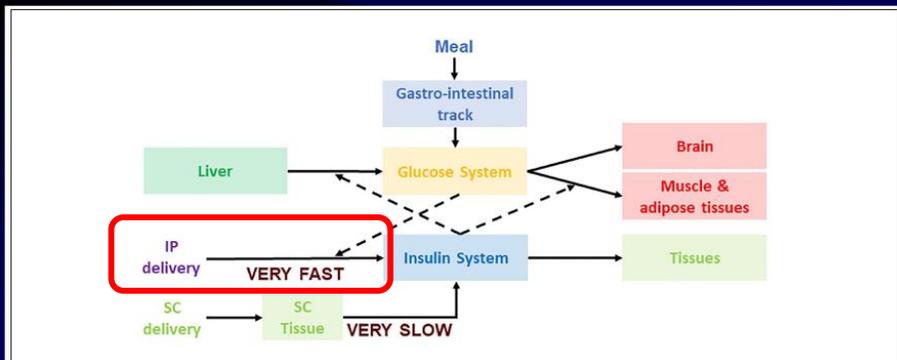


Figure 6. A schematic view of subcutaneous vs intraperitoneal insulin delivery.

