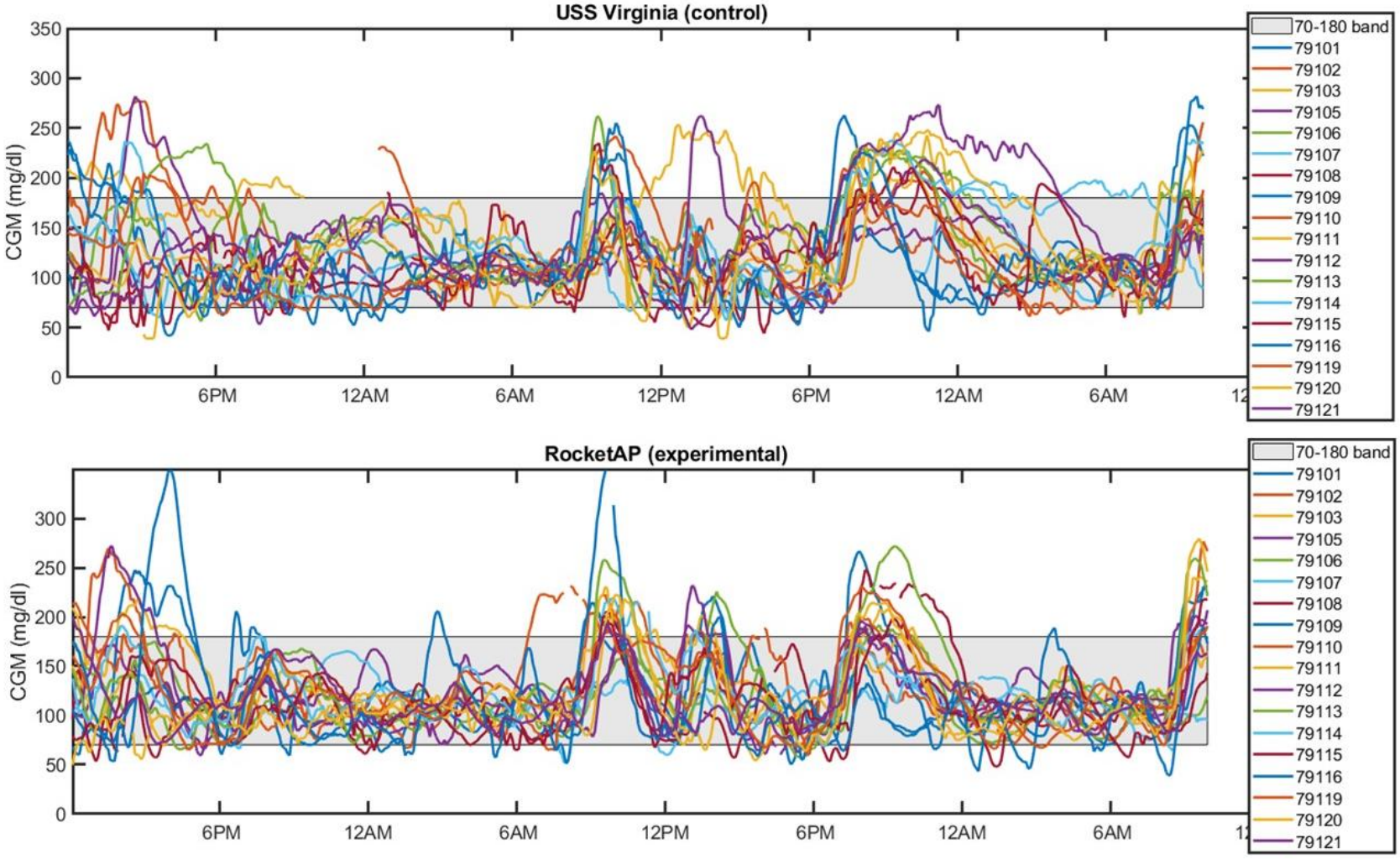
SUPPLEMENTAL MATERIAL

Supplementary Figure 1: Glucose tracings for individual study participants over a 46-hour period by closed loop control system. In both cases, the announced dinner was at 6 pm the first day on that system and the unannounced dinner was at 6 pm the second day on the system.



Supplementary Table 1: Participant characteristics

Characteristic	mean±SD, except as noted	[range]
Age (years)	15.6±1.6	[13-20]
Gender female-male	9:9 (ratio)	N.A.
Weight (kg)	65.2±11.5	[43, 96]
Height (cm)	166.6±8.9	[151, 183]
BMI	23.4±3.4	[18.7, 29.3]
Duration of diabetes (years)	7.7±3.2	[3.3, 17.7]
HbA1c (%)	7.4±1.5	[5.8, 12.6]
TDI (IU)	59.6±16.3	[28, 99]
TDU (IU)	64.8±22.6	[27, 113]
Carbohydrate ratio (g per IU)	7.7 ± 1.9	[4.7,10]
Correction factor (mg/dL per IU)	43±18	[20,100]
TIR from home data (%)	60.0±17.3	[22.8, 87.9]
Average basal rate (U/hr)	1.3±0.4	[0.5 – 2.2]

Abbreviations: IU, injected units;TDI, total daily insulin; TIR, time in range 70-180 mg/dL; SD, standard deviation.

Supplementary Table 2. Glycemic outcomes [dinnertime + 12h]

	Unannounced dinner (Secondary outcomes)			Announced dinner (Secondary outcomes)		
	USS	RCKT	P-value	USS	RCKT	P-value
Glycemic metrics						
Mean CGM glucose (mg/dL)	145±25	123±11	**<0.001[a]**	116.5±20	110.2±7.5	0.1
% CGM time < 50 mg/dL (<2.8 mmol/L)	0 [0-0]	0 [0-0]	1	0 [0-0]	0 [0-0]	1
% CGM time < 60 mg/dL (<3.3 mmol/L)	0 [0-0]	0 [0-0]	0.26	0 [0-0]	0 [0-0]	0.08
% CGM time < 70 mg/dL (<3.9 mmol/L)	0 [0-0.7]	0 [0-1.2]	0.54	0.7 [0-4.9]	0 [0-2]	0.14
% CGM time 70-140 mg/dL (3.9-7.8 mmol/L)	52 [42-64]	73 [70-76]	**0.004[b]**	83 [56-90]	89 [78-96]	**0.03[b]**
% CGM time 70-180 mg/dL (3.9-10.0 mmol/L)	75 [58-83]	90 [79-96]	**<0.001[b]**	95 [91-99]	100 [97-100]	**0.007[b]**
% CGM time > 180 mg/dL (>10.0 mmol/L)	25 [14-37]	8.7 [3-17]	**0.003[b]**	0 [0-1.2]	0 [0-0]	0.11
% CGM time > 250 mg/dL (>13.9 mmol/L)	0 [0-0]	0 [0-0]	0.52	0 [0-0]	0 [0-0]	1
% CGM time > 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)	41±9.2	36±14	0.06	23±8	21±6.3	0.25
CGM CV (%)	29±6.5	29±11	0.56	20±5	19±6	0.32
Safety metrics						
Severe hypoglycemia (number of events)	0 [0-0]	0 [0-0]	1[b]	0 [0-0]	0 [0-0]	1[b]
Diabetes ketoacidosis (number of events)	0 [0-0]	0 [0-0]	1[b]	0 [0-0]	0 [0-0]	1[b]
Technical performance metrics						
Percent time in CLC (%)	97±7	100±1	0.16	93±14	100±2	0.14
Total injected insulin (IU)	20±4	21±8	0.28	17.5±5	17±5	0.33

Significance levels <0.05 are presented in bold font.
a One-sided paired t-test
b Wilcoxon signed-rank test
Abbreviations: CV, coefficient of variation; CGM, continuous glucose monitor; CLC, closed-loop control; IQR, interquartile range; IU, injected units; RCKT, RocketAP system; SD, standard deviation; USS, Unified Safety System.

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Supplementary Table 3. Overall glycemic control (46 hours, 12PM day 1 to 10 AM day 3).

Secondary outcomes			
	USS	RCKT	P-value
Glycemic metrics			
Mean CGM glucose (mg/dL)	128±15.5	121.6±7.5	**0.05**[a]
% CGM time < 50 mg/dL (<2.8 mmol/L)	0 [0-0]	0 [0-0]	1
% CGM time < 60 mg/dL (<3.3 mmol/L)	0 [0-0.5]	0 [0-0.3]	0.14
% CGM time < 70 mg/dL (<3.9 mmol/L)	2.9 [0.9-4.8]	2.2 [1 - 3.6]	0.22
% CGM time 70-140 mg/dL (3.9-7.8 mmol/L)	65 [55-71]	73 [66-77]	**0.01**[b]
% CGM time 70-180 mg/dL (3.9-10.0 mmol/L)	81 [76-86]	86 [82-92]	**0.007**[b]
% CGM time > 180 mg/dL (>10.0 mmol/L)	14 [7-18]	9.5 [5-13]	**0.03**[b]
% CGM time > 250 mg/dL (>13.9 mmol/L)	0 [0 - 1.5]	0 [0-1.0]	0.49
% CGM time > 300 mg/dL (>16.7 mmol/L)	0 [0-0]	0 [0-0]	1
CGM SD (mg/dL)	40.4±7.7	38±9.5	0.17
CGM CV (%)	32±4.6	31±7.7	0.41
Safety metrics			
Severe hypoglycemia (number of events)	0 [0-0]	0 [0-0]	1
Diabetes ketoacidosis (number of events)	0 [0-0]	0 [0-0]	1
Technical performance metrics			
Percent time in CLC (%)	95±7.4	99±1.3	**0.004**[b]
Total injected insulin (IU)	85±20	78±23	**0.01**[a]

Significance levels <0.05 are presented in bold font.
a One-sided paired t-test
b Wilcoxon signed-rank test
Abbreviations: CV, coefficient of variation; CGM, continuous glucose monitor; CLC, closed-loop control; IQR, interquartile range; IU, injected units; RCKT, RocketAP system; SD, standard deviation; USS, Unified Safety System.

Supplementary Table 4. Individual participants' data on Time-in-range (TIR) and time <70 mg/dL: pre-study and during each controller.

Participant	% TIR (70-180 g/dL)					% time < 70 mg/dL				
	Baseline	RCKT		USS		Baseline	RCKT		USS	
		Announced day	Unannounced day	Announced day	Unannounced day		Announced day	Unannounced day	Announced day	Unannounced day
79101	87.9	71.9	78.8	86.1	75.4	2.4	5.9	3.4	5.9	8.3
79102	22.8	70.1	93.9	97.9	88.3	0.2	0.0	0.0	0.0	5.7
79103	58.3	78.8	83.7	54.9	56.1	0.2	0.0	0.0	0.0	0.0
79105	87.2	98.3	81.8	94.1	95.5	6.9	1.0	6.4	5.6	4.2
79106	39.4	100.0	81.8	97.9	69.7	0.5	0.0	4.6	1.4	0.8
79107	77.0	95.5	95.8	96.5	50.0	1.1	4.2	3.4	3.1	1.9
79108	67.2	87.5	71.2	85.4	78.0	3.3	8.0	9.9	11.8	14.0
79109	79.6	100.0	90.9	78.1	96.2	3.3	0.0	1.9	12.9	2.3
79110	52.7	85.17	88.3	47.2	82.2	0.4	3.5	1.1	0.7	0.0
79111	54.0	92.0	92.1	97.6	75.8	0.1	0.4	3.0	0.4	1.9
79112	46.8	88.2	81.8	86.1	80.3	0.3	1.4	1.1	0.7	0.0
79113	71.9	89.9	79.2	78.5	84.1	0.6	2.8	0.0	1.0	0.0
79114	55.0	89.2	94.7	89.9	67.8	0.1	0.0	0.4	0.4	1.5
79115	46.5	95.1	89.4	69.4	82.2	0.9	2.4	2.7	5.2	1.9
79116	64.4	72.9	78.0	81.6	78.8	1.5	8.7	17.1	2.4	7.2
79119	60.5	91.7	79.2	87.5	86.7	0.1	1.4	6.1	4.9	3.8
79120	41.6	88.2	84.1	74.3	68.6	3.2	4.2	2.3	7.3	5.7
79121	66.9	94.8	98.1	98.6	53.8	0.3	0.0	0.0	1.0	4.9

Abbreviations: RCKT, RocketAP system; USS, Unified Safety System.

Supplementary Table 5. Glycemic outcomes overnight (11:00PM-7:00AM).

Secondary outcomes			
	USS	RCKT	P-value
Glycemic metrics			
Mean CGM glucose (mg/dL)	123±20	106.4±7.3	**0.002**[a]
% CGM time < 50 mg/dL (<2.8 mmol/L)	0 [0-0]	0 [0-0]	1
% CGM time < 60 mg/dL (<3.3 mmol/L)	0 [0-0]	0 [0-0]	0.26
% CGM time < 70 mg/dL (<3.9 mmol/L)	0 [0-3.8]	0 [0-3.7]	0.47
% CGM time 70-140 mg/dL (3.9-7.8 mmol/L)	76.3 [58.5-87.4]	95.3 [90.4-100]	**<0.001**[b]
% CGM time 70-180 mg/dL (3.9-10.0 mmol/L)	92.2 [81.2-96]	99.2 [95.7-100]	**<0.001**[b]
% CGM time > 180 mg/dL (>10.0 mmol/L)	5 [0-9.8]	0 [0-0]	**0.002**[b]
% CGM time > 250 mg/dL (>13.9 mmol/L)	0 [0-0]	0 [0-0]	1
% CGM time > 300 mg/dL (>16.7 mmol/L)	0 [0-0]	0 [0-0]	1
CGM SD (mg/dL)	28±9.7	18.1±7.2	**0.004**[a]
CGM CV (%)	22±5.7	7±7	**0.01**[a]
Safety metrics			
Severe hypoglycemia (number of events)	0 [0-0]	0 [0-0]	1
Diabetes ketoacidosis (number of events)	0 [0-0]	0 [0-0]	1
Technical performance metrics			
Percent time in CLC (%)	96±7	99±2	0.07
Total injected insulin (IU)	15±4	14±5	0.34

Significance levels <0.05 are presented in bold font.
a One-sided paired t-test
b Wilcoxon signed-rank test
Abbreviations: CV, coefficient of variation; CGM, continuous glucose monitor; CLC, closed-loop control; IQR, interquartile range; IU, injected units; RCKT, RocketAP system; SD, standard deviation; USS, Unified Safety System.

Supplementary Table 6. Hypoglycemic events/treatments

Secondary outcomes			
	USS	RCKT	P-value
Overall (46 hours)	4.5 [1-8]	3 [1 – 5]	0.14
DT - DT+6h (Unannounced)	0 [0-0]	0 [0-0]	0.26
DT - DT+6h (Announced)	0 [0-1]	0 [0-1]	0.11
DT - DT+12h (Unannounced)	0 [0-1]	0 [0-0.7]	0.41
DT - DT+12h (Announced)	1 [1-2]	0 [0-1]	0.13
Overnight	0 [0-2.8]	0 [0-1.7]	0.43

Significance levels <0.05 are presented in bold font.
a One-sided paired t-test
b Wilcoxon signed-rank test
Abbreviations: DT, dinner time; RCKT, RocketAP system; USS, Unified Safety System.

Supplementary Table 7. Cumulative Bolus Priming System (BPS)

			Cumulative BPS	
Subject	TDI	Time of first BPS injection after meal (min)	BPS 1h (%TDI)	BPS 2h (%TDI)
79101	56	11	3.93 (7)	3.93 (7)
79102	100	37	5.00 (5)	5.00 (5)
79103	73	24	3.65 (5)	3.65 (5)
79105	76	14	3.81 (5)	3.81 (5)
79106	44	20	1.32 (3)	1.32 (3)
79107	27	N.A.	0.00 (0)	0.00 (0)
79108	54	N.A.	0.00 (0)	0.00 (0)
79109	69	16	2.07 (3)	2.07 (3)
79110	53	18	1.69 (3)	1.69 (3)
79111	71	49	2.13 (3)	2.13 (3)
79112	46	30	1.38 (3)	1.38 (3)
79113	100	37	3.00 (3)	3.13 (3)
79114	46	28	1.38 (3)	1.38 (3)
79115	71	24	3.55 (5)	3.55 (5)
79116	44	N.A.	0.00 (0)	0.00 (0)
79119	100	23	6.00 (6)	6.00 (6)
79120	50	54	1.63 (3)	1.63 (3)
79121	66	18	1.98 (3)	1.98 (3)

N.A. (not applicable), indicates that no BPS injection was provided for that particular meal.

Bolus Priming System (BPS)

The BPS integrates to the core MPC system as a dosing module that punctually commands comparatively large amounts of insulin computed as fractions of TDI, fractions that progressively increase with the estimation of the *"probability of a large glycemic disturbance occurring in the last 30 min"*. The BPS module runs every 5 min with the procedure detailed as follows:

a. A 2nd order polynomial is fitted onto the last 30-min worth of CGM data where the coefficients p1, p2, and p3 are generated.
b. The coefficients in (a) are used as features in a logistic regression classification algorithm that detects postprandial periods. This classification algorithm was trained with data collected for a previous study. [1]
c. The disturbance probability at each iteration, π_k, is found using the following equation

$$\pi_k = \frac{1}{1 + e^{-y_{log}}}$$

with y_{log} the output from the logistic regression classifier.

d. This probability is then used to determine if a bolus is required and if so, how much insulin should be delivered. The bolus priming system has a predetermined schedule for what percent of the individual's TDI amount should be ad-ministered at each probability threshold. Before an amount is delivered, the amount of insulin on board from antecedent bolus priming doses is subtracted. This dose is computed as

$$J_{\mathrm{BPS}} = \max\left(\mathrm{P}_{\mathrm{TDI}} \cdot \mathrm{TDI} - \frac{\mathrm{IOB}_{BPS}}{\mathrm{TDI}}, 0\right)$$

where J_{BPS} is the amount of insulin commanded by the BPS, $\mathrm{P}_{\mathrm{TDI}}(\%)$ is the percentage of the patient's TDI requested based on the dosing schedule belowIOB_{BPS}

$$\mathrm{P}_{\mathrm{TDI}} = \begin{cases} 3\% & \text{if } 0.3 \le \pi_k < 0.5 \\ 5\% & \text{if } 0.5 \le \pi_k < 0.7 \\ 6\% & \text{if } 0.7 \le \pi_k < 0.9 \\ 7\% & \text{if } \pi_k \ge 0.9 \end{cases}$$

IOB_{BPS} accounts for the active insulin in the circulation as per previous BPS injections using a 6h-insulindecaying curve.

The disturbance probability thresholds together with their corresponding insulin doses were determined through the use of a method that has been employed before to "replay" past real data using regularized deconvolution to solve for unknown inputs into the glucose-insulin model.[2]

1. Garcia-Tirado J, Brown SA, Laichuthai N, et al. Anticipation of Historical Exercise Patterns by a Novel Artificial Pancreas System Reduces Hypoglycemia During and After Moderate-Intensity Physical Activity in People with Type 1 Diabetes. *Diabetes Technol Ther.* 2020.
2. Hughes J, Gautier T, Colmegna P, Fabris C, Breton MD. Replay Simulations with Personalized Metabolic Model for Treatment Design and Evaluation in Type 1 Diabetes. *J Diabetes Sci Technol.* 2020:1932296820973193.