

Insulin Pump Therapy

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Disclosures

- Member of Clinical Advisory Panel for Tandem
- Work on a variety of clinical trials funded by or supported by Medtronic

Objectives

- Discuss insulin pumps, features, and who may benefit from their use.
- Patient selection, education, and resources.
- Discuss insulin pump therapy in different populations:
 - Newly diagnosed
 - T2DM
 - Pregnancy
 - Children
- Review common patterns in glycemic control in people on insulin pump therapy.
- Strategies for optimization of pump therapy now and in the future

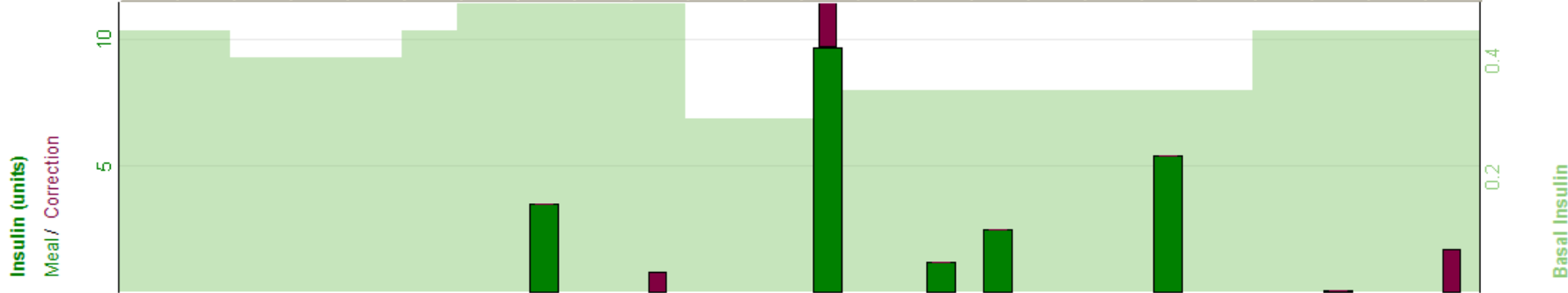
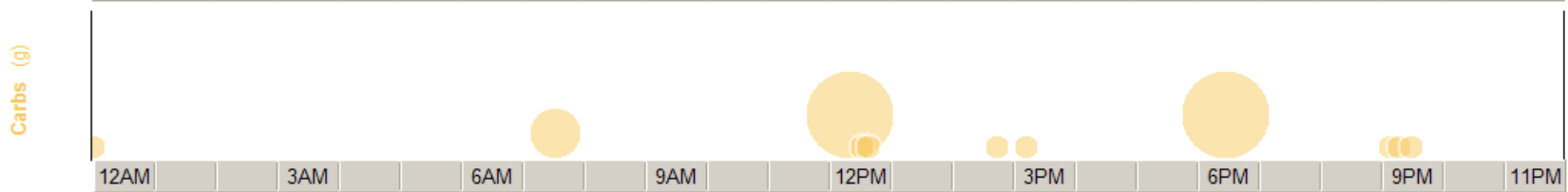
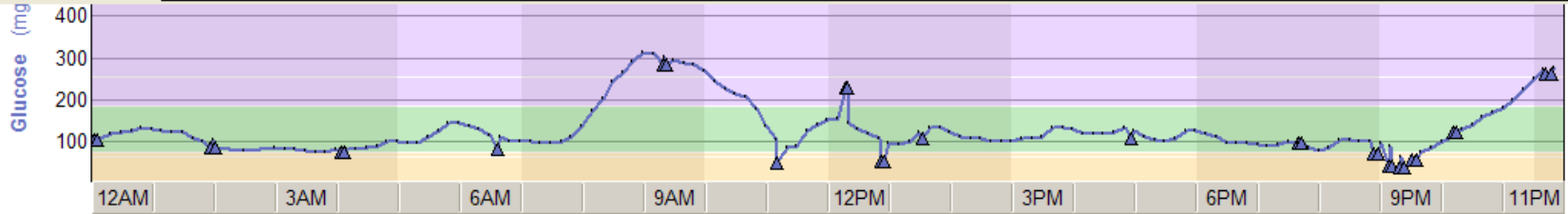
Why Pump Therapy?

- Less injections
- Flexibility in eating, exercise, and sleeping
- Bolus calculator and IOB/BOB
- More fun
- More physiologic
- Enables fine-tuning of insulin doses
- Software can provide accurate record of doses and often BG



Pizza at 12 Noon...Who Knew?

Statistics | **Daily Combination** | Weekly Pump | Glucose Modal Day



	12AM		3AM		6AM		9AM		12PM		3PM		6PM		9PM		11PM	Total/Summary							
Glucose	*104	*125	*83	*82	*75	*100	*144	*100	*135	*313	*267	*135	*152	*96	*122	*101	*127	*126	*125	*91	*79	*95	*101	*181	
Carbs	4						35			116	15	30		65											345
Corr Bolus	0.00	0.00			0.00				0.85				1.80							0.00	0.00	*0.00	0.00	1.75	4.40
Meal Bolus	0.00						3.50			*7.50	1.25	2.50		5.40								*0.10			22.40
Total Bolus							3.50		0.85				11.45	1.25	2.50				5.40				0.10	1.75	26.80
Basal	0.45	0.45	0.40	0.40	0.40	0.45	0.50	0.50	0.50	0.50	0.30	0.30	0.33	0.35	0.35	0.35	0.35	0.35	0.35	0.45	0.45	0.45	0.45	0.45	9.73
Total Insulin	0.45	0.45	0.40	0.40	0.40	0.45	0.50	4.00	0.50	1.35	0.30	0.30	11.78	0.35	1.60	2.85	0.35	0.35	5.75	0.35	0.45	0.55	0.45	2.20	36.53

Insulin Pump Therapy...

- A recent Cochrane review of 23 RCTs with 976 participants with T1D compared CSII and MDI (at least 3 injections per day).
 - There was a statistically significant mean difference in HbA1c of -0.3% in CSII users.
 - Reduced occurrence of severe hypoglycemia in CSII users
 - Improved QofL measures in CSII users

Pump Therapy in Pregnancy

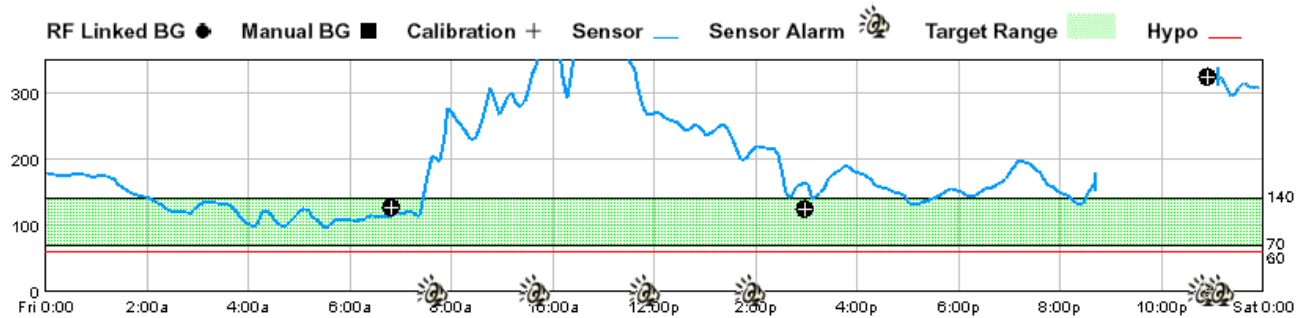
- In pregnancy, achieving normoglycemia is paramount
- Clinical trials are challenging to conduct in this population
- Pump therapy is best started pre-conception, recommend not starting in the first trimester.
- Due to heightened concern for hyperglycemia and DKA in pregnancy paper suggests using NPH at hs and adjusting insulin accordingly.

Potential Pitfalls in Pump Therapy

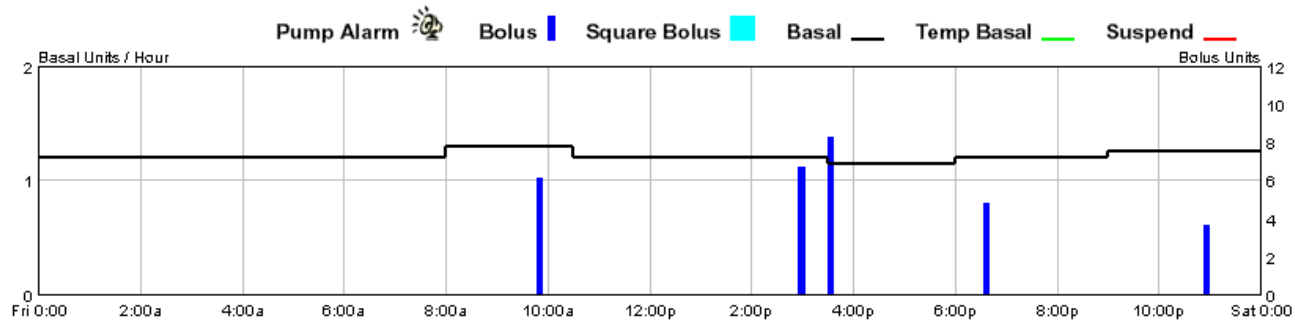
- Risk of DKA
- There is an additional device to wear/ use
- Cost
- Solid foundation in diabetes education is key
- You must use it for it to be effective!

13 y.o. male, A1c=8.8, Daily Summary

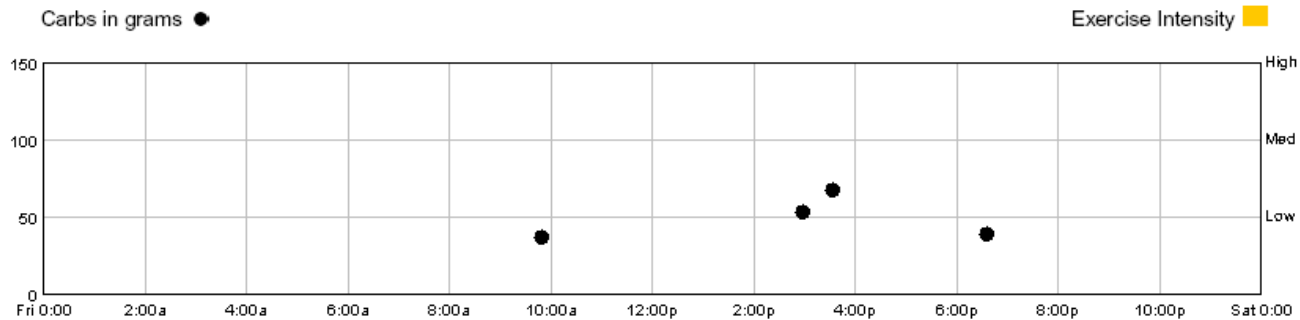
Glucose (mg/dL)



Insulin Delivery



Carbohydrates and Exercise

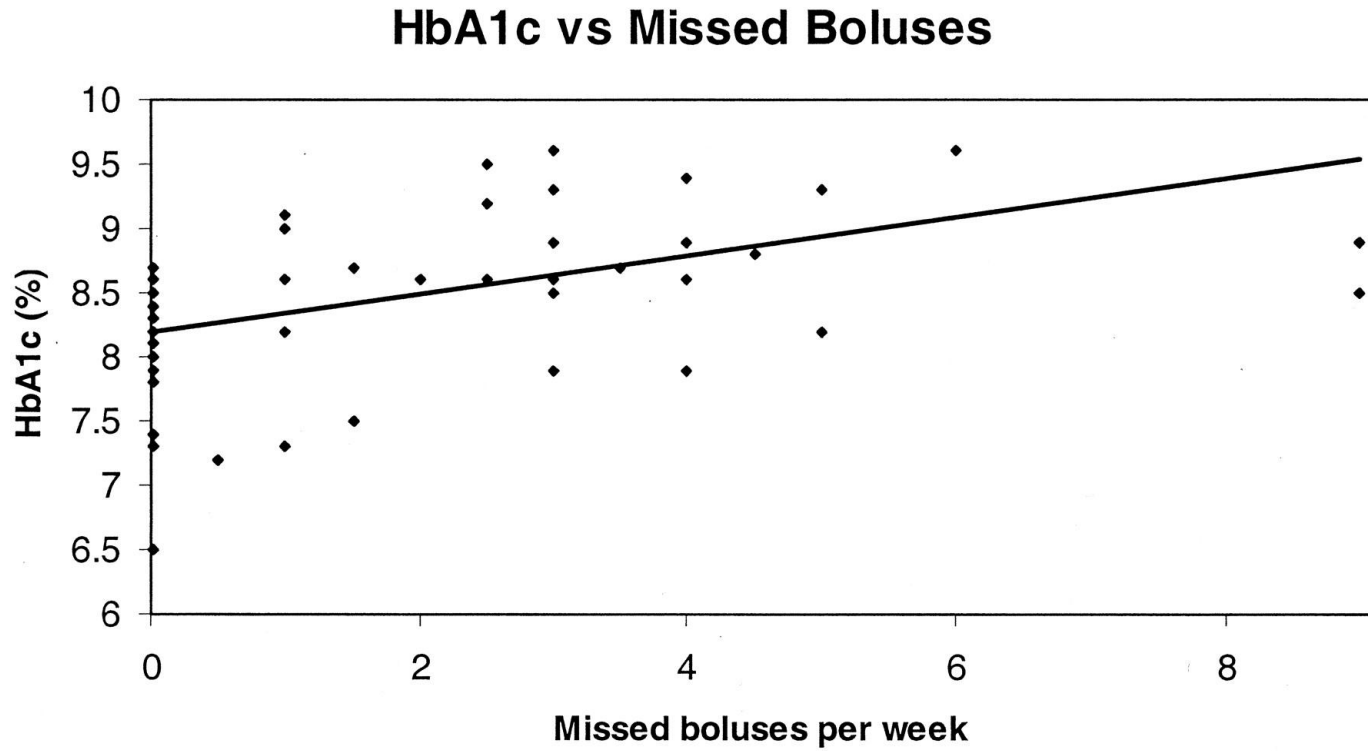


Missed Meal Bolus

Burdick, Chase, Pediatrics 113: e221, 2004

- 65% missed more than 1 meal bolus/week
- 2 missed meal bolus/week caused A1c to increase $\frac{1}{2}\%$

Fig 1. HbA1c levels correlated with the number of missed meal insulin boluses per day (r = .4)








Burdick, J. et al. Pediatrics 2004;113:e221-e224



INSULIN PUMPS: 1978 - 1987



"Have you thought about an insulin pump upgrade?"

Pump	Reservoir Size	Basal	Smallest Bolus Increment	Food Database	Integrated BG Meter	Integrated CGM
	315 units	0.1-25 u/hr 0.1 u/incr	0.1	Yes, PDA	No	No
	300 units	0.1-16 u/hr 0.1 u/incr	0.1 up to 10 1 unit for 10-87 u	No	No	No
	523: 176 u 723: 300 u	0.025- 35 u/hr 0.025 u/ incr	0.025 upto 0.975 ➤0.975 0.05	No	Yes OT Ultra Link	Yes
	200 units	0.05-30 u/hr 0.05 u/incr	0.05	Yes in PDM	Yes, FreeStyle Meter in PDM	No
	200 units	0.025- 25 u/hr 0.025 u/ incr	0.05	Yes, Meter Remote	Yes, OT Ultra Ping	No

At what age should CSII be initiated?

- My take: At any age person with diabetes and if applicable the family seem ready, willing and able to do so.
- At younger ages care must be taken to be sure that there is adequate training and provision for management of pump.
 - Daycare
 - School
 - Babysitter
 - Safety with the pump itself (lockout etc)

Pump Therapy in Youth: SEARCH Study

- The largest review to date focused on insulin pump therapy in children and adolescents (N=2,743) found that pump therapy was associated with the lowest A1c levels across all ages.

Paris, C. A., Imperatore, G., Klingensmith, G., Petitti, D., Rodriguez, B., Anderson, A.M., Schwartz, I.D., Standiford, D.A., Pihoker, C. (2009). Predictors of insulin regimens and impact on outcomes in youth with type 1 diabetes: the SEARCH for diabetes in youth study. *Journal of Pediatrics*, 155, 183-189.

Starting CSII Early Is Not New...

- Over 20 years ago, an RCT evaluated the impact of a 2 week trial of CSII in newly diagnosed adolescents with T1D:
 - Resulted in both improved metabolic control and beta cell preservation 1 year later than participants on MDI
 - (Shah et al., 1989)
- A smaller RCT pilot trial (N=24) of kids 8-18 years of age compared MDI to CSII started with in 1 month of diagnosis:
 - Trend of increased c-peptide over 1 year in CSII but not statistically significant
 - Improved glycemic control, was well tolerated and had higher reported patient satisfaction.
 - (Thraikill et al., 2011)

Shah, S. C., Malone, J.I., Simpson, N.E. (1989). A randomized clinical trial of intensive insulin therapy in newly diagnosed insulin-dependent diabetes mellitus. *New England Journal of Medicine*, 320, 311-320.

Thraikill, K. M., Moreau, C.S., Swearingen, C, Rettiganiti, M., Edwards, K., Morales, A.E., Kemp, S.F., Frindik, P., Fowlkes, J.L. (2011). Insulin pump therapy started at the time of diagnosis: effects on glycemic control and pancreatic beta cell function in type 1 diabetes. *Diabetes Technology and Therapeutics*, 13(10), 1023-1030. doi: 10.1089/dia.2011.0085

My experience....

- Currently I work on a study that starts newly diagnosed adults and children on an artificial pancreas followed by CGM and CSII use within 7 days of diagnosis of T1D.
 - While a challenging time to learn both families and children
 - Flexibility of therapy is helpful especially at the time of diagnosis when glucose and insulin needs are variable.
 - Injection or pen technique is still critical but not facing multiple injections is often a big motivator for kids and parents.
 - Using pump that can assist in calculations is often helpful at this time (IOB/ BOB).

What happens over-time?

- A retrospective chart review of 113 youth with T1D on pump therapy for up to 7 years found that:
 - Baseline HbA1c of $\leq 7.5\%$
 - Duration of T1D ≤ 1 year
 - Younger age at initiation of pump therapy
 - All were independently associated with Lower HbA1c during long-term follow up.

Pinhas-Hamiel, O., Tzadok, M., Hirsh, G., Bokyo, V., Graph-Barel, C., Lerner-Geva, L., Reichman, B. (2010). The Impact of Baseline Hemoglobin A1c Levels Prior to Initiation of Pump Therapy on Long-Term Metabolic Control. *Diabetes Technology and Therapeutics*, 12(7), 567-573.

When to start CSII?

- When the person with diabetes decides it is the best option for them and when in your opinion they are ready.
 - Testing BG frequently (at least 4-6 x day).
 - Able to count carbohydrates
 - Able to identify patterns and initiate changes in therapy
 - Demonstrate ability to program pump and prepare and insert infusion set .
 - Able to verbalize risk mitigation and management of DKA.
 - Reliable with follow up.

Potential Sources of Variability in Pump Therapy

1. CARBS: How many carbs?



- Double Double with Onion
- French Fries
- Chocolate Shake

Survey Says

- Which of the following is your best estimate of the total number of carbs in this meal?
 - a. 103 grams
 - b. 136 grams
 - c. 165 grams
 - d. 181 grams
- Would you consider this high fat and or high protein?
- How would you bolus for this meal?
 - Normal
 - Extended
 - Dual 50/50
 - Dual 70/30
 - Dual other

Nutritional Facts State...

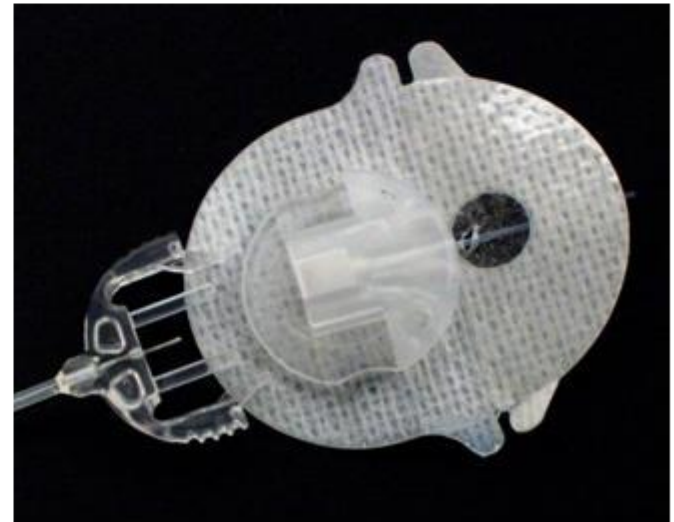
Food	Grams of CHO	Grams of Fat	Grams of Protein
Double Double with Onion	39	41	37
French Fries	54	18	7
Chocolate Shake	72	29	10
TOTAL	165	88	54



2. INFUSION

Infusion Sets and Site Location

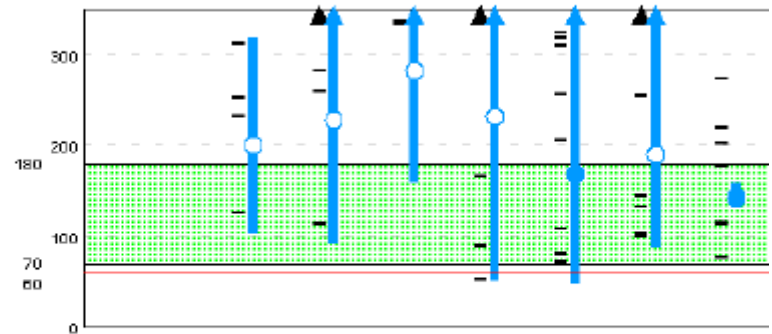
- Variability in speed of absorption
- Variability in patency of infusion set (kinking or crystallization)
- Variability in tissue
- Variability by frequency of infusion set change



Frequency of Site Changes

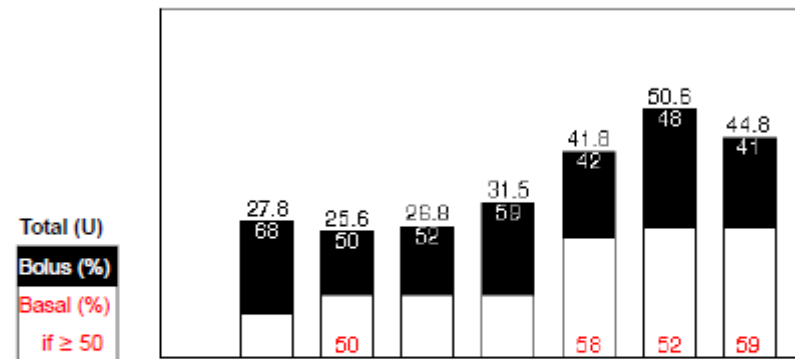
Glucose - High / Low / Average (mg/dL)

In Range ● Out of Range ○ Meter (BG) — Sensor (SG) | Target F



BG/SG Stats	Mon Oct 17	Tue Oct 18	Wed Oct 19	Thu Oct 20	Fri Oct 21	Sat Oct 22	Sun Oct 23	Mon Oct 24
Average	0	230/200	255/228	335/282	271/232	209/168	182/189	168/142
High	0	311/318	365/379	336/400	596/400	324/359	357/359	273/158
Low	0	125/103	114/90	333/158	52/51	71/47	99/87	78/131
Standard Dev.	NA	NA/60	NA/66	NA/60	215/98	102/86	94/54	65/5
# of Readings	0	4/195	4/195	4/288	5/261	8/423	6/401	7/29
#Hypo Excurs.	0	0/0	0/0	0/0	1/1	0/1	0/0	0/0

Insulin Delivery (Units)



	Mon Oct 17	Tue Oct 18	Wed Oct 19	Thu Oct 20	Fri Oct 21	Sat Oct 22	Sun Oct 23	Mon Oct 24
Total Insulin	0	27.8	25.6	26.8	31.5	41.8	50.6	44.8
Basal Insulin	0	9	12.8	12.8	12.8	24.4	26.5	26.5
Bolus Insulin	0	18.8	12.8	14	18.7	17.4	24.1	18.3
# of Boluses	0	9	7	11	5	14	14	9
Average Bolus Fill Amount	NA	2.1	1.8	1.3	3.7	1.2	1.7	2

3. BOLUS TIMING

Initial Data:



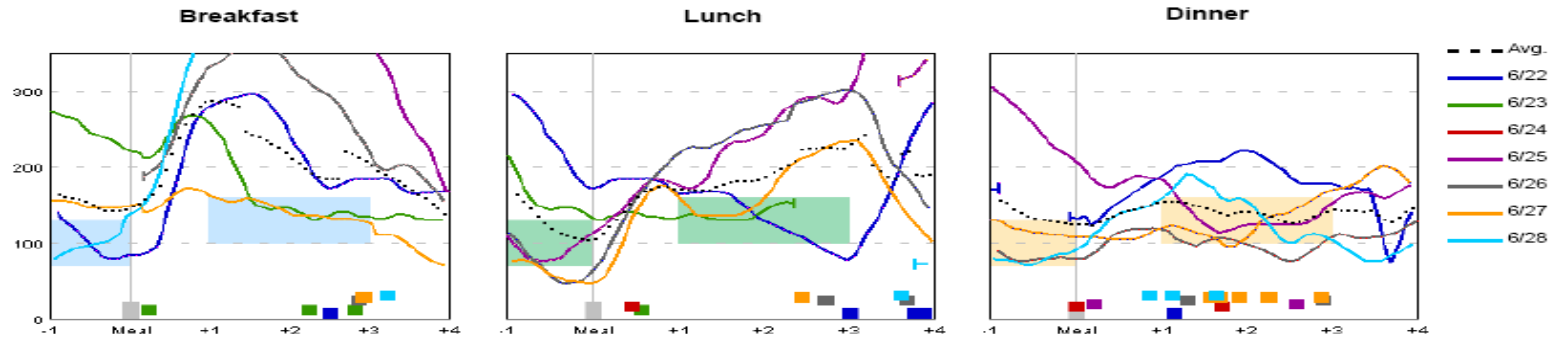
Jun 22 - Jun 28, 2007
(7 days)

HbA1c: No Data

Pump: Paradigm 722
Sensor: In use

#414689

Overlay by Meal Event (mg/dL)



	Sleeping 3:00 AM - 6:00 AM	Before Breakfast	After Breakfast	Before Lunch	After Lunch	Before Dinner	After Dinner	Evening 11:00 PM - 3:00 AM	All Time Periods
Range	100 - 150	70 - 130	100 - 160	70 - 130	100 - 160	70 - 130	100 - 160	100 - 150	
Average SG	202	150	230	123	192	135	140	142	168
High SG	368	274	400	296	302	306	222	370	400
Low SG	58	80	128	46	78	70	76	44	44
Standard Dev.	104	64	89	71	62	73	40	90	88
# of Readings	143	48	105	60	113	51	120	211	851

TDD= 40 units

I:CHO Ratio at Breakfast 1:10 grams all other meals 1:12 grams

Delivers bolus immediately before or just after the start of the meal.

3 Months Later: Boluses 5-15 min Pre-Meal Unless Low..



Oct 4 - Oct 10, 2007

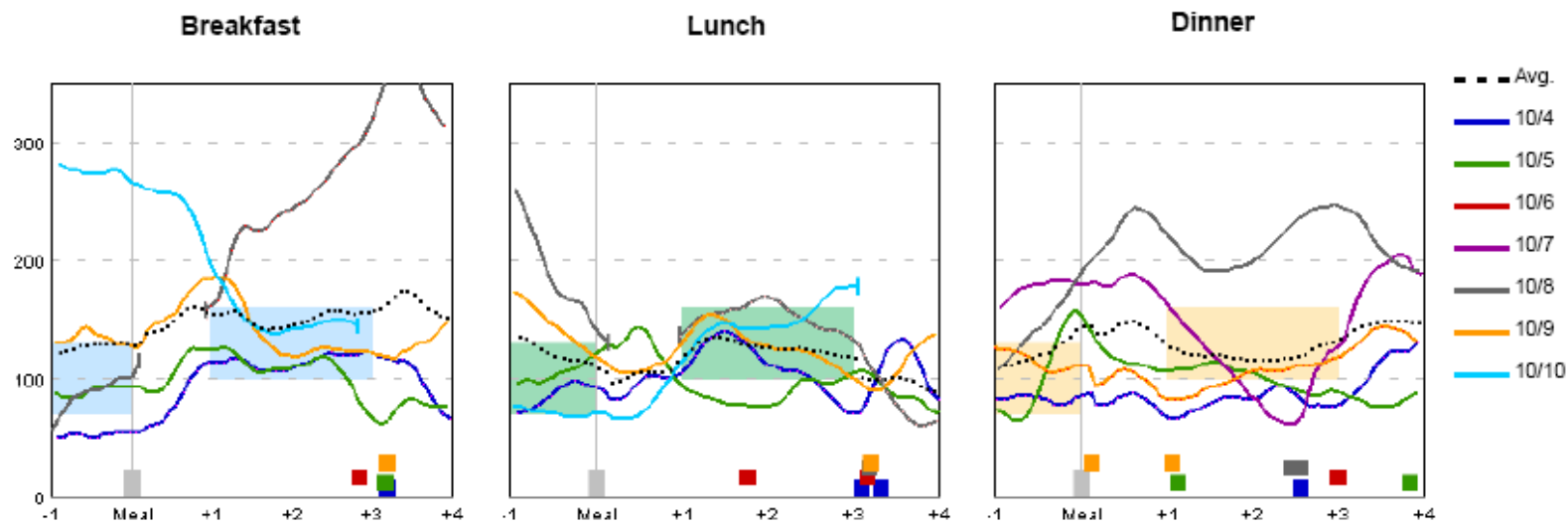
(7 days)

HbA1c: No Data

Pump: Paradigm 722
Sensor: In use

#414689

Overlay by Meal Event (mg/dL)



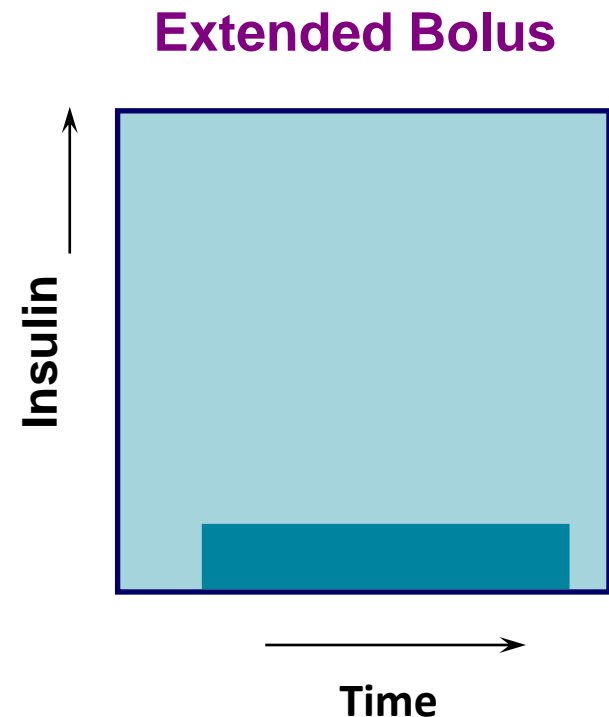
	Sleeping 3:00 AM - 6:00 AM	Before Breakfast	After Breakfast	Before Lunch	After Lunch	Before Dinner	After Dinner	Evening 11:00 PM - 3:00 AM	All Time Periods
Range	100 - 150	70 - 130	100 - 160	70 - 130	100 - 160	70 - 130	100 - 160	100 - 150	
Average SG	152	127	151	120	126	123	120	234	156
High SG	282	282	308	260	178	184	248	334	334
Low SG	40	50	70	68	70	64	62	148	40
Standard Dev.	79	79	54	48	28	39	51	46	70
# of Readings	180	60	118	60	120	60	120	195	913

4. Type of Food and Bolus

When Would I Use a
Dual or Square Wave Bolus?

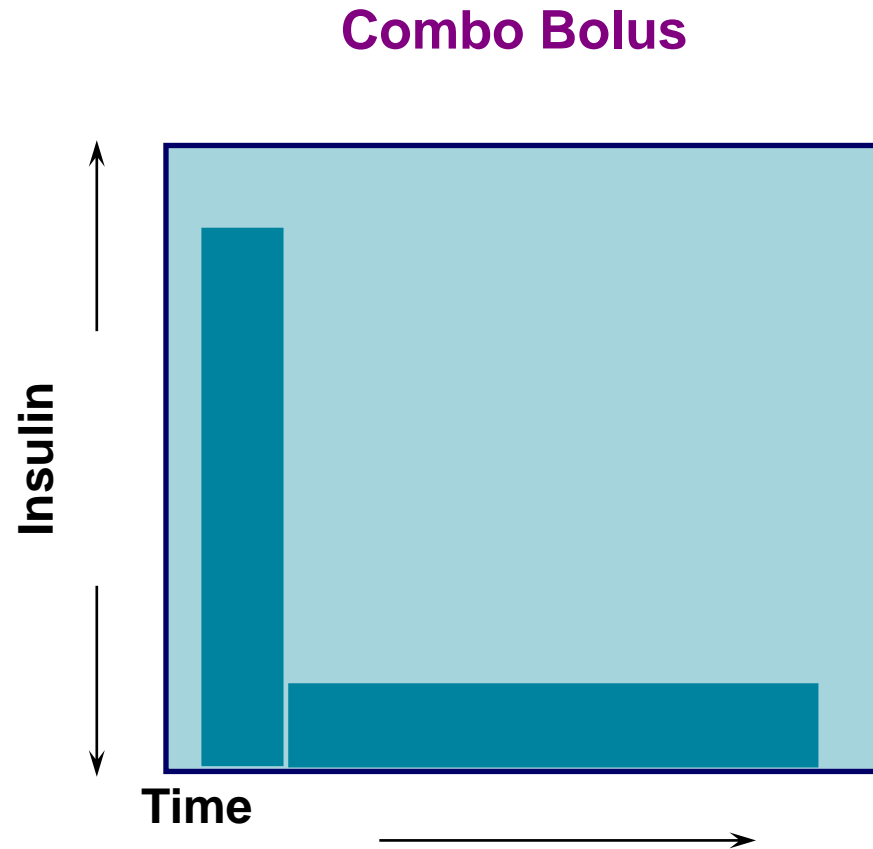
Extended/ Square Wave Bolus

- Delivers insulin evenly over a programmed time
- Potential uses:
 - Gastroparesis
 - Very low carb meal that is high in fat/ protein
- You can deliver a “normal” bolus while you are delivering an extended bolus



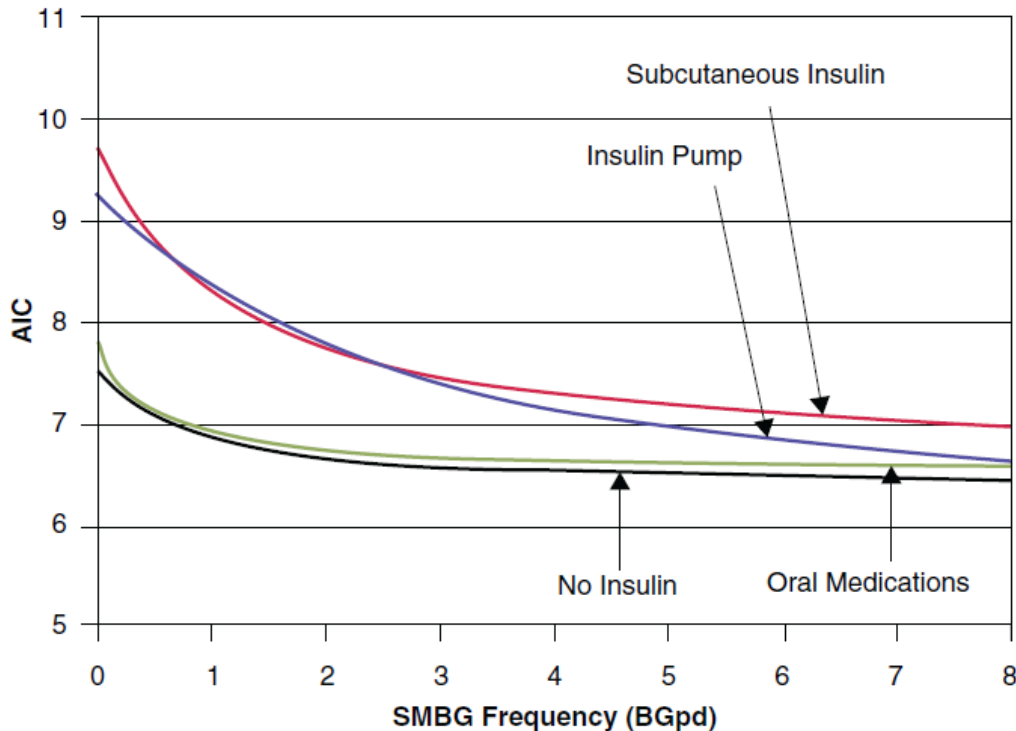
Combo/Dual Wave Bolus

- A combination of a normal bolus plus an extended bolus
- Potential uses:
 - Meals that are high in fat/ protein but have carbs
 - Gastroparesis



5. Frequency of BG Testing

Mathematical Model to Predict Effects of SMBG Frequency on HbA1c



- N= 1, 255 subjects

- Patients on CSII benefitted the most from increased frequency of BG testing

Davidson, P. C., Bode, B.W., Steed, R.D., Hebblewhite, H.R., . (2007). A cause-and-effect-based mathematical curvilinear model of that predicts the effects of self-monitoring of blood glucose frequency on HbA1c and is suitable for statistical correlations. *Journal of Diabetes Science and Technology*, 1, 850-856.

Hirsch, I. B. (2010). Practical Pearls in Insulin Pump Therapy. *Diabetes Technology and Therapeutics*, 12(1), S-23-S-27.

6. Education

Suggestions for Education

- Online pump trainings by manufacturer
- Favorite for patients:
 - Hans

CASE STUDIES

What's New and Next in Pump Therapy



t:slim™

Features at a Glance



Color Touch Screen



300 Unit Cartridge



Micro-Delivery Technology



Rechargeable Battery



USB Connectivity

Therapy Management System



t:connect™

Slide courtesy of Tandem

t:slim™ Insulin Delivery System

Bolus Screen – Entering a BG value



The image shows a digital keypad interface for entering a blood glucose (BG) value. At the top, there are three buttons: "BACK" on the left, "Enter BG" in the center, and "DONE" on the right. Below these buttons, the unit "mg/dL" is displayed. The keypad consists of a 4x3 grid of buttons. The first three rows contain the digits 1 through 9. The fourth row contains the digit 0 and a "DEL" button. The "DONE" button is highlighted in blue.

BACK	Enter BG	DONE
mg/dL		
1	2	3
4	5	6
7	8	9
	0	DEL

t:slim™ Insulin Delivery System

Bolus Screen

The screenshot displays the Bolus Screen interface for the t:slim Insulin Delivery System. At the top, there are three buttons: 'BACK' on the left, a central numeric input field containing '3.6', and 'NEXT' on the right. Below the input field, the unit 'units' is displayed. The screen is divided into two columns: 'CARBS' on the left and 'BG' on the right. Under 'CARBS', the value '30' is shown in large blue font, with 'grams' below it. Under 'BG', the value '127' is shown in large blue font, with 'mg/dL' below it. At the bottom of the screen, there is a wide button labeled 'View Calculation'.

BACK	3.6	NEXT
	units	
CARBS	BG	
30	127	
grams	mg/dL	
View Calculation		

mySentry Components



Monitor



Outpost



Power Supply

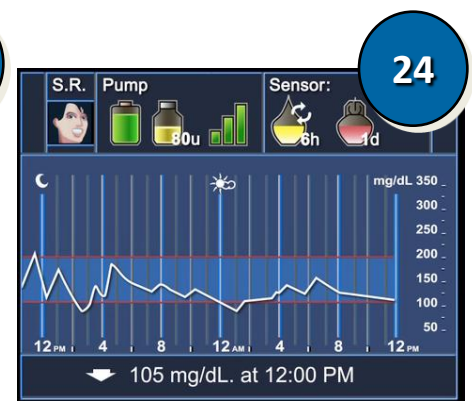
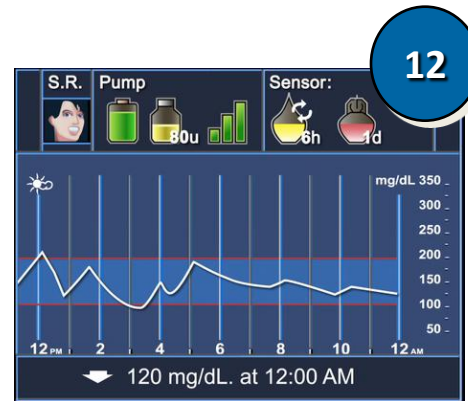
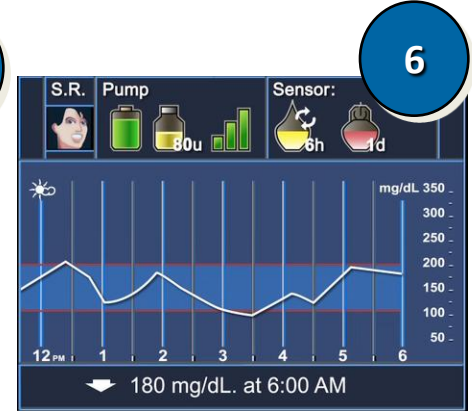
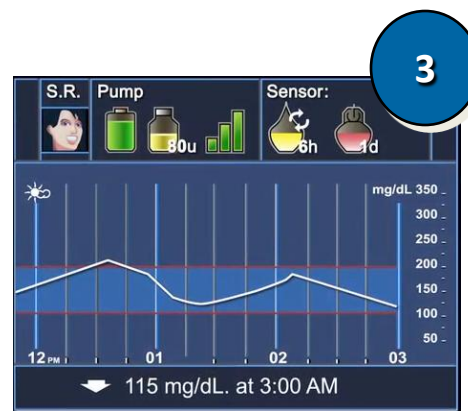
Slide Courtesy of Medtronic

Glucose Snapshot Screen



Slide Courtesy of Medtronic

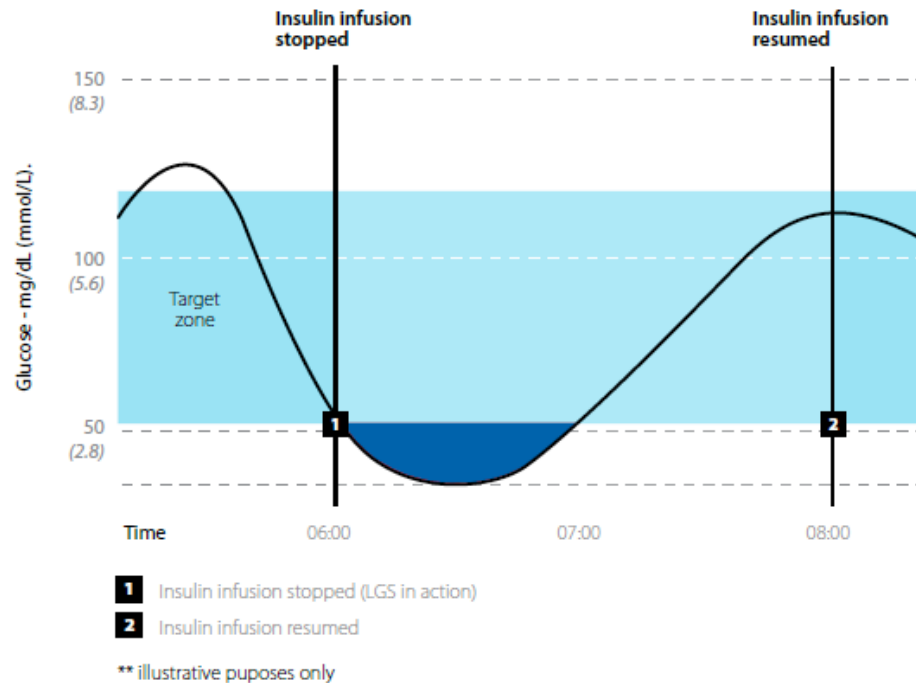
Sensor Glucose Graphs



Slide Courtesy of Medtronic

Baby Steps.. Medtronic Veo: LGS

*The Low Glucose Suspend in focus***



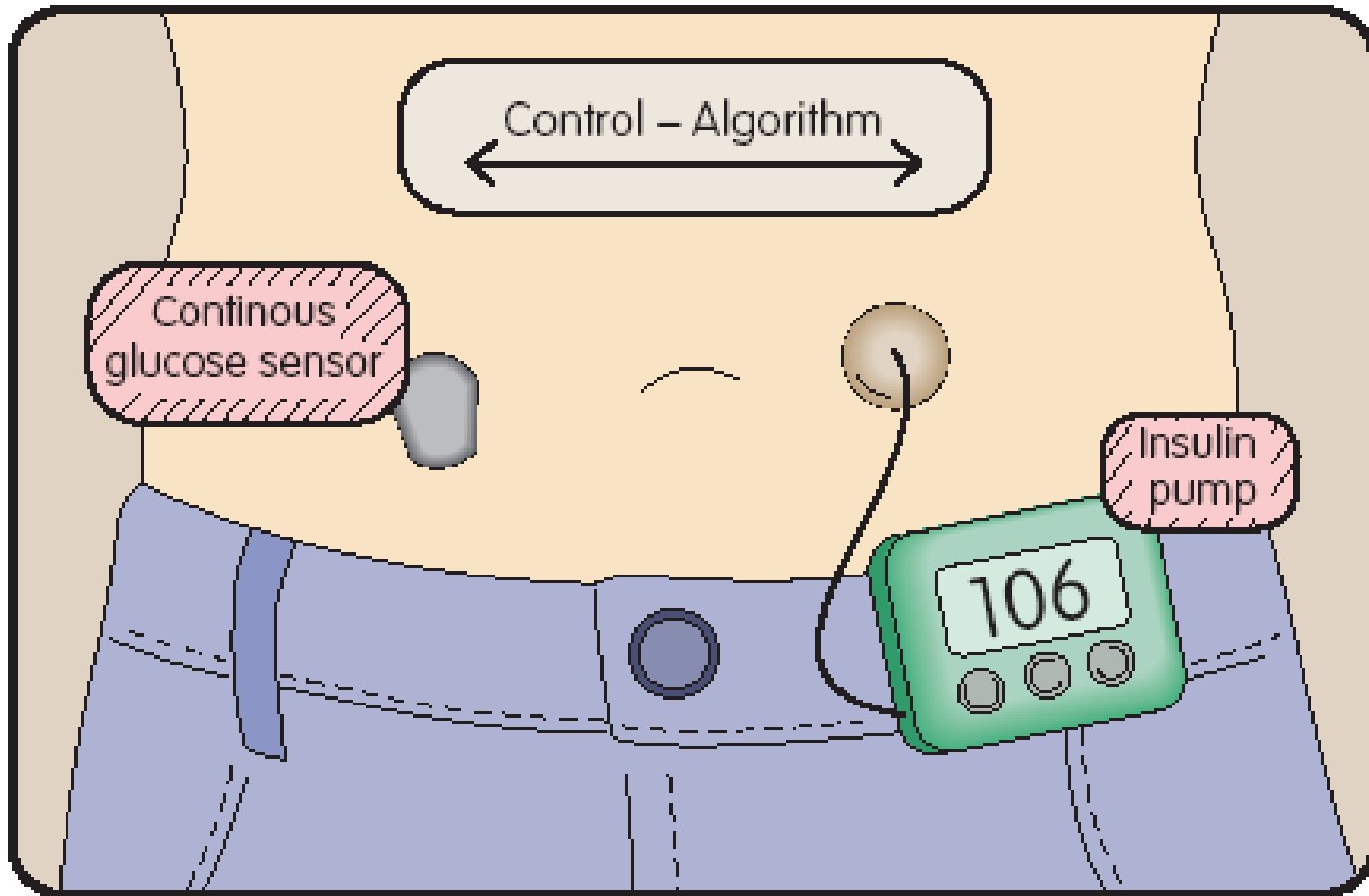
7. Bode B, Gross K, Rikalo N, Schwartz S, Wahl T, Page C, Gross T, Mastrototaro J. Alarms Based on Real-Time Sensor Glucose Values Alert Patients to Hypo- and Hyperglycemia: The Guardian Continuous Monitoring System. *Diabetes Technol Ther.* 2004;6(2):105-113.

8. Garg S, Zisser H, Schwartz S. et. al, Improvements in glycaemic excursions with a transcutaneous, real-time continuous glucose sensor. *Diabetes Care.* 2006. 29:44-50.



<http://insulin.neru9.com/images/insulin-pump-price-cost.jpg>

What is an Artificial Pancreas?



???? Questions ?????

- THANK YOU
- Email: jblock@stanford.edu