Artificial Pancreas Technologies:
New Tools to Improve Diabetes Care Today and Tomorrow

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University of Virginia
Center for Diabetes Technologies
October 2017
Learning Objectives

1) List the mechanical components of an artificial pancreas system.
2) List commercially-available systems with progressively added features of artificial pancreas technology.
3) Identify 3 sources of delay inherent to how an AP system responds to blood glucose excursions.
Disclosures

1) I have no relevant financial disclosures related to the content of this presentation.

2) Many of the Artificial Pancreas technologies presented are not currently approved by the FDA (outside of research protocols).
The landscape of Type 1 diabetes...
The landscape of Type 1 diabetes...
The landscape of Type 1 diabetes...

“I want my old pancreas back!”

- No worry about hypoglycemia.
- Food flexibility.
- No blood sugar checking.
- Sports without distraction.
- A good night’s sleep.
The landscape of Type 1 diabetes...

“What do I need to do to get a consistently normal blood sugar?!?”

Barriers:
• Variability in food.
• Variability in activity.
• Variability in symptoms.
• Variability in communication.
• High HbA1c’s.
• Sub-optimal sleep.
The landscape of Type 1 diabetes...

“What do I need to do to get a consistently normal blood sugar?!?”

Barriers:
• Variability in food.
• Variability in activity.
• Variability in symptoms.
• Variability in communication.
• High HbA1c’s.
• Sub-optimal sleep.
The landscape of Type 1 diabetes...

Real, circa 1984

- Urine glucose
- No blood glucose meters
- Insulin pumps rare
- Insulins with overnight peaks
The landscape of Type 1 diabetes...

Real, circa 1960

- Pig insulin
- Follow symptoms only
- No home glucose assessments
The Previous Century

- Backpack insulin & glucagon pump
- **Intravenous glucose control:** Albisser et al; Mirouze, Selam et al; Pfeiffer et al.
- Subcutaneous Continuous Glucose Monitoring: Minimed CGMS, 1999
- Blood glucose meters & insulin pumps becoming smaller
- Models of diabetes becoming larger & more complex
- First use of Insulin pumps: Tamborlane et al; Pickup et al.
- Insulin discovered: Frederick Banting
- Ames Reflectance Meter
- The Auto Syringe (Dean Kamen)
The Artificial Pancreas 40 Years Ago
Trying to bridge the chasm...
Insulin pumps:

Up-sides
• Variation of basal insulin delivery
• Painless delivery for smaller doses

Down-sides
• More things to go wrong
• Attached to hardware 24-7
CGM:

Up-sides

• View trends—predict lows/highs
• Alarm to wake for lows overnight

Down-sides

• Need to calibrate
• Delay in reading, not as accurate
• Teens: cost/benefit
Basic Design of AP Systems

- Insulin Delivery
- Insulin Request
- Insulin Pump
- Traditional Insulin Delivery
Basic Design of AP Systems

Glucose: CGM

Insulin Parameters: basal rate, carb ratio, correction factor, total daily insulin

Insulin-on-Board

Insulin Decision

\[
\begin{align*}
\dot{G}_p &= -k_2 G_p + k_1 G_t - U_{ii} - E_t + k_{p1} - k_{p2} G_p - k_{p3} I_d + \frac{f \cdot k_{abs} Q_{gut}}{BW} \\
\dot{G}_t &= -k_1 G_t + k_2 G_p - \frac{(V_{m0} + V_{mX} \cdot X) G_t}{K_{m0} + G_t} \\
\dot{G}_{sc} &= -k_{sc} \left( G_{sc} - \frac{G_p}{V_g} \right) \\
\dot{I}_p &= -(m_2 + m_4) I_p + m_1 I_l + k_{a1} I_{sc1} + k_{a2} I_{sc2} \\
\dot{I}_l &= -(m_1 + m_3) I_l + m_2 I_p \\
\dot{I}_d &= -k_i (I_d - I_1) \\
\dot{\hat{X}} &= -p_{2u} \left( X - \left( \frac{I_p}{V_i} - I_b \right) \right) \\
\dot{I}_{sc1} &= -k_d I_{sc1} - k_{a1} I_{sc1} + \frac{J(t)}{BW} \\
\dot{I}_{sc2} &= k_d I_{sc2} - k_{a2} I_{sc2} \\
\dot{Q}_{sto1} &= -k_{gri} Q_{sto1} + M(t) \\
\dot{Q}_{sto2} &= -k_{empt} Q_{sto2} + k_{gri} Q_{sto1} \\
\dot{Q}_{gut} &= k_{abs} Q_{gut} + k_{empt} Q_{sto2}
\end{align*}
\]
Basic Design of AP Systems

Glucose: CGM

Insulin Parameters: basal rate, carb ratio, correction factor, total daily insulin

Insulin-on-Board

Insulin Decision

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\begin{align*}
\dot{G}_p &= -k_2 G_p + k_1 G_l \\
\dot{G}_l &= -k_1 G_l + k_2 G_p \\
\dot{G}_{sc} &= -k_{sc} \left( G_{sc} - \frac{G_p}{V} \right) \\
\dot{I}_p &= -\left( m_2 + m_4 \right) \dot{G}_p \\
\dot{I}_l &= -\left( m_1 + m_3 \right) \dot{G}_l \\
\dot{I}_i &= -k_i \left( I_1 - \frac{I_p}{V_i} \right) \\
\dot{I}_d &= -k_i (I_d - I_1) \\
\dot{X} &= -p_{2u} \left( X - \left( \frac{I_p}{V_i} - I_b \right) \right) \\
\dot{I}_{sc1} &= -k_d I_{sc1} - k_{a1} I_{sc1} + \frac{J(t)}{BW} \\
\dot{I}_{sc2} &= k_d I_{sc2} - k_{a2} I_{sc2} \\
\dot{Q}_{sto1} &= -k_{gri} Q_{sto1} + M(t) \\
\dot{Q}_{sto2} &= -k_{empt} Q_{sto2} + k_{gri} Q_{sto1} \\
\dot{Q}_{gut} &= k_{abs} Q_{gut} + k_{empt} Q_{sto2}
\end{align*}
\]
Basic Design of AP Systems

- “Closed Loop” Control
UVa’s DiAs: the Diabetes Assistant

System Status

User Touch Controls

Hypoglycemia Traffic Light

USS Messages

Hyperglycemia Traffic Light
UVa’s DiAs: the Diabetes Assistant

Plot screen

- CGM trace
- Bolus marker
- Basal profile
- Basal delivery
UVa’s DiAs: the Diabetes Assistant

Devices worn by the subject

- Dexcom G4 Sensor
- Tandem t:slim insulin pump

Devices near the subject

- DiAs Smart Phone
- Bluetooth Wireless connection
- Dexcom G4 Receiver

Wireless using Dexcom Share
AP Strategy-Iterative: Increases in Automation

Kowalski AJ. Can we really close the loop and how soon? Accelerating the availability of an artificial pancreas: A roadmap to better diabetes outcomes. *Diabetes Technol Ther*, 11:S113-S119, 2009

- **Very Low Glucose Insulin Off Pump**
- **Hypoglycemia Minimizer**
- **Hypoglycemia/ Hyperglycemia Minimizer**
- **Safety System**
- **USS Virginia**
- **Fully Automated Multi-Hormone Closed Loop**
- **Fully Automated Insulin Closed Loop**
- **Automated Basal / Hybrid Closed Loop**
- **Meal Control Module**

END
Threshold suspend: Medtronic

A Glycated Hemoglobin

<table>
<thead>
<tr>
<th>Glycated Hemoglobin (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>At randomization</td>
</tr>
<tr>
<td>7.26 ± 0.71</td>
</tr>
</tbody>
</table>

B Mean AUC for Nocturnal Hypoglycemic Events

<table>
<thead>
<tr>
<th>AUC (mg/dL x min)</th>
<th>Run-in phase</th>
<th>Study phase</th>
<th>38% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold-Suspend Group</td>
<td>1547 ± 2035</td>
<td>1406 ± 1995</td>
<td>1568 ± 1995</td>
</tr>
<tr>
<td>Control Group</td>
<td>980 ± 1200</td>
<td>1200</td>
<td></td>
</tr>
</tbody>
</table>

C Sensor Glucose <70 mg/dL

<table>
<thead>
<tr>
<th>Percent</th>
<th>60 to &lt;70 mg/dL</th>
<th>50 to &lt;60 mg/dL</th>
<th>&lt;50 mg/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocturnal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Threshold-suspend group</td>
<td>3.0</td>
<td>1.8</td>
<td>1.2</td>
</tr>
<tr>
<td>Control group</td>
<td>3.1</td>
<td>2.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Day and Night Combined</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Threshold-suspend group</td>
<td>2.8</td>
<td>2.5</td>
<td>1.6</td>
</tr>
<tr>
<td>Control group</td>
<td>3.7</td>
<td>2.8</td>
<td>1.9</td>
</tr>
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Predictive suspend: Medtronic MiniMed 640G
Predictive suspend: Medtronic

Low BG’s: 21% nights pLGS
33% control
Randomized cross-over design; two 5-day sessions

Control condition: CGM + pump (usual control)
Experimental condition: Daytime – CGM + pump; Nighttime – closed-loop control (11PM-7AM);

No meal restrictions; Alcohol permitted; No intensive exercise; Driving restricted to 25 miles during the day;

Primary Outcome: Time within target range 80-150 mg/dl at wakeup (7AM);

Control Algorithm: USS Virginia with nightly “system (person) reset” to target of 120mg/dl at 7AM

N=40 participants
Overnight: Average glucose was reduced by ~30mg/dl; Percent time in target increased by 25%. No adverse events.

Bedside AP: Nighttime glucose control

<table>
<thead>
<tr>
<th>Time in 80-150 mg/dl</th>
<th>Open-loop (mean; quartiles)</th>
<th>Closed-loop (mean; quartiles)</th>
</tr>
</thead>
<tbody>
<tr>
<td>42.6% (OL)</td>
<td>49.5% (CL)</td>
<td></td>
</tr>
<tr>
<td>Time in 70-180 mg/dl</td>
<td>38.5% (OL)</td>
<td>82.4% (CL)</td>
</tr>
</tbody>
</table>
# Bedside AP: Outcomes

40 participants closed-loop vs. sensor-augmented pump therapy

<table>
<thead>
<tr>
<th></th>
<th>Sensor-Augmented Pump</th>
<th>Closed-Loop Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Blood Glucose at 7AM</td>
<td>145.3</td>
<td>123.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Average Blood Glucose overall</td>
<td>147.0</td>
<td>142.0</td>
<td>NS</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent time within 80-140mg/dl</td>
<td>42.9%</td>
<td>51.7%</td>
<td>0.001</td>
</tr>
<tr>
<td>Percent time below 70mg/dl</td>
<td>4.3%</td>
<td>2.5%</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Overnight Control Correlated with Control the Next Day ($r=0.4$, $p=0.008$):
Challenges: Missed meal/snack

**UVA** (Danny Cherñavsky, Mark DeBoer, Marc Breton, Boris Kovatchev)

Adolescents age 12-17 years

- Admission
  - 30 gram snack without insulin
- 11:00
- Lunch with under-bolus of insulin
- 12:00
- Discharge
  - Lunch with under-bolus of insulin

---

**Admission**

- 08:00
- 30 gram snack without insulin
- 09:00
- 10:00
- 11:00

**Lunch with under-bolus of insulin**

- 12:00
- 13:00
- 14:00
- 15:00
- 16:00
- 17:00
Challenges: Missed meal/snack

Cherňavvsky, DeBoer et al. Ped Diab 2014
Challenges: Missed meal/snack

Cherñavvsky, DeBoer et al. Ped Diab 2014
Challenges: Missed meal/snack

Median and Quartile Glucose Traces for AP (red) and Usual Care (Blue)

Cherñavvsky, DeBoer et al. Ped Diab 2014
Challenges: Missed meal/snack

Conclusions:

1. The AP can eventually compensate for missed insulin for food, but it takes time.

2. For tight control, some mealtime identification is likely here to stay for now.

Cherňavvsky, DeBoer et al. Ped Diab 2014
Challenges: Exercise

UVA (Marc Breton, Sue Brown, Stacey Anderson, Boris Kovatchev)

Time Course of the Deviation from Plasma Glucose at Onset of Exercise (glucose drop)

- Standard Control-to-Range
- Heart Rate enhanced Control-to-Range

Deviation from initial exercise BG [mg/dL]

Time since start of exercise [min]

Breton Diab Tech Ther 2014
Challenges: Exercise

UVA (Marc Breton, Sue Brown, Stacey Anderson, Boris Kovatchev)

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Time Course of the Deviation from Plasma Glucose at Onset of Exercise (glucose drop)

- Glucose: CGM
- Insulin Parameters: BR, CR, CF, TDD
- Heart rate monitor
- Insulin-on-Board

Model: State Estimates → Glucose Prediction → Insulin Decision

Deviation from initial exercise BG [mg/dL]

Time since start of exercise [min]
Challenges: Exercise

**UVA** (Marc Breton, Sue Brown, Stacey Anderson, Boris Kovatchev)

**Time Course of the Deviation from Plasma Glucose at Onset of Exercise (glucose drop)**

- **Standard Control-to-Range**
- **Heart Rate enhanced Control-to-Range**

**Deviation from initial exercise BG [mg/dL]**

**Time since start of exercise [min]**

Breton Diab Tech Ther 2014
AP Challenges: Exercise

UVA, VCU (Mark DeBoer, Gary Francis, Marc Breton); Funding

Adolescents age 12-17 years, randomized cross-over:
AP and exercise with & without heart rate monitor input

Exercise cycle:
15 min 5 15 min 5 15 min
HR goal: 140

Admission to research unit, begin AP

08:00 10:00 12:00 14:00 16:00 18:00 20:00 22:00 24:00 02:00 04:00 06:00 08:00

Light breakfast Lunch Dinner Snack Discharge

Sleep

DeBoer Ped Diab 2016
Challenge: Exercise

UVa (Marc Breton, Mark DeBoer), VCU (Gary Francis)

DeBoer Ped Diab 2016
Challenge: Snow skiing

UVa (Marc Breton, Boris Kovatchev), Barbara Davis (David Maahs)

TO BOLDLY GO WHERE NO CLOSED LOOP HAS GONE BEFORE

January 2016: Five-Day Ski Camp on Closed-Loop Control
Wintergreen, Virginia, elevation 3,515’ (1,071 meters);

April 2016: Five-Day Ski Camp on Closed-Loop Control
Breckenridge, Colorado, elevation 12,840’ (3,914 meters)

NIDDK DP3 DK 106826 (2015-19)
Challenge: Snow skiing

UVa (Marc Breton, Boris Kovatchev), Barbara Davis (David Maahs)

Average glucose and interquartile range:

<table>
<thead>
<tr>
<th>Activity</th>
<th>Experimental</th>
<th>Control</th>
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<tbody>
<tr>
<td>Overall time in range (70-180mg/dl)</td>
<td>71.3%</td>
<td>64.7%</td>
</tr>
<tr>
<td>Time in range second half of night, 3-7AM</td>
<td>84.6%</td>
<td>66.2%</td>
</tr>
<tr>
<td>Time below 70 mg/dl</td>
<td>1.8%</td>
<td>3.2%</td>
</tr>
</tbody>
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Breton Diab Care 2017
Challenge: Young children

UVa (Mark DeBoer, Daniel Chernavsky)

12 children age 5-8 years

Families arrive to resort; young child AP system placed

Meals, activities

Sleep

Day 1

Day 2

Day 3

Day 4

AP system removed, family discharged

DeBoer Diab Tech & Ther 2017
Challenge: Young children

UVa (Mark DeBoer, Daniel Chernavsky)

12 children age 5-8 years

Families arrive to resort; young child AP system placed

Screening visit; CGM sensor placed

Day -3 Day -2 Day -1 AP Camp Day +1 Day +2 Day +3

Home care Day 1 Day 2 Day 3 Day 4 Home care

Meals, activities

Sleep

Pump, BG information downloaded, CGM sent back

AP system removed, family discharged

DeBoer Diab Tech & Ther 2017
Challenge: Young children

UVa (Mark DeBoer, Daniel Chernavsky)

12 children age 5-8 years

Families arrive to resort; young child AP system placed
Meals, activities
Sleep
Meals, activities
Sleep
AP system removed, family discharged

Day 1
Day 2
Day 3
Day 4

DeBoer Diab Tech & Ther 2017
Challenge: Young children

UVa (Mark DeBoer, Daniel Chernavsky)

Differences adjusted for total steps:
** p<0.01
*** p<0.001
NS p>0.05

Total events <70 per participant:
AP 3.3 ±1.0
Home 4 ±1.0

DeBoer DTT 2017
Results: Mean BG

**Mean Glucose**
- AP period: 152 mg/dL
- Home care period: 190 mg/dL

***Significant difference***

**Total Daily Insulin**
- AP period: 18.6 units/d
- Home care period: 19.9 units/d

NS = Not statistically significant

DeBoer DTT 2017
Results: Lock-out screens

• 0/12 parents reported that their child discovered the password or were found entering insulin doses or settings unsupervised.
Bedside AP: at home

Artificial Pancreas:

- **31106**
  - Hypo: 99 mg/dL (19 minutes ago)
  - Stopped
  - Hyper: 100%
  - Recent note: No note
  - No alert

- **31107**
  - Hypo: 145 mg/dL (22 minutes ago)
  - Stopped
  - Hyper: 97%
  - Recent note: No note
  - No alert

- **31108**
  - Hypo: 100 mg/dL (7 minutes ago)
  - Stopped
  - Hyper: 99%
  - Recent note: No note
  - No alert

- **31109**
  - Hypo: 98 mg/dL (22 minutes ago)
  - Stopped
  - Hyper: 96%
  - Recent note: No note
  - No alert

- **31110**
  - Hypo: 133 mg/dL (24 minutes ago)
  - Stopped
  - Hyper: 99%
  - Recent note: No note
  - No alert

Pump/CGM only:

- **30010001**
  - Hypo: 127 mg/dL (8 minutes ago)
  - Pump Mode
  - Hyper: 99%
  - Recent note: No note
  - No alert

- **30010002**
  - Hypo: 132 mg/dL (3 minutes ago)
  - Pump Mode
  - Hyper: 98%
  - Recent note: No note
  - No alert

- **30010003**
  - Hypo: 189 mg/dL (3 minutes ago)
  - Pump Mode
  - Hyper: 85%
  - Recent note: No note
  - No alert

- **30010004**
  - Hypo: 240 mg/dL (8 minutes ago)
  - Pump Mode
  - Hyper: 99%
  - Recent note: No note
  - No alert

- **30010005**
  - Hypo: 149 mg/dL (4 minutes ago)
  - Pump Mode
  - Hyper: 99%
  - Recent note: No note
  - No alert
Dual-hormone system

Boston U: (El-Khatib, Russell, Magyar, Sinha, McKeon, Nathan, Damiano)

Requires:

Glucose: CGM

Insulin Parameters: BR, CR, CF, TDD

Insulin-on-Board

Glucagon Decision

Model: State Estimates

Glucose Prediction

Fully Automated Multi-Hormone Closed Loop

Fully Automated Insulin Closed Loop

Manual meal-time bolus eliminated

Automated Basal / Hybrid Closed Loop

Closed loop at all times with meal-time manual assist bolusing

Very Low Glucose
Insulin Off Pump

Pump shuts off when user not responding to low-glucose alarm

Hypoglycemia
Minimizer

Predictive hypoglycemia causes alarm followed by reduction or cessation of insulin delivery below low threshold

Hypoglycemia/
Hypoglycemia Minimizer

Same as Product #2 but added feature allowing insulin dosing above high threshold (e.g., 200mg/dl)
Dual-hormone system

**Boston U:** (El-Khatib, Russell, Magyar, Sinha, McKeon, Nathan, Damiano)

- **A**
  - Adults, AMB (solid traces) versus Adolescents, AMB (dashed traces)
  - Venous PG, mg/dl

- **B**
  - CGM glucose, mg/dl

- **C**
  - Dosed insulin, mU per kg

- **D**
  - Plasma insulin levels, µIU/ml

- **E**
  - Plasma glucagon levels, pg/ml

**Mealtime glucagon**

**Total insulin ↑ 20%**

El-Khatib JCEM 2014
Recent Closed-Loop Studies at a Glance

<table>
<thead>
<tr>
<th>Source of Data</th>
<th>Medtronic 670G safety trial</th>
<th>JDRF Pilot trial of long-term closed-loop control</th>
<th>Home use of bihormonal bionic pancreas</th>
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<tr>
<td>Duration of Closed-Loop Control</td>
<td>3 months</td>
<td>6 months</td>
<td>11 days</td>
</tr>
<tr>
<td>Number of participants</td>
<td>124</td>
<td>30 (Phase 1) 14 (Phase 2)</td>
<td>39</td>
</tr>
<tr>
<td>Algorithm Automation</td>
<td>Basal Rate Only</td>
<td>Basal Rate and Correction Boluses</td>
<td>Insulin + Glucagon</td>
</tr>
<tr>
<td>Algorithm Description</td>
<td>PID with insulin feedback</td>
<td>Model-based sliding target</td>
<td>-</td>
</tr>
<tr>
<td>Sensor/Pump</td>
<td>Medtronic MiniMed 670G System</td>
<td>Dexcom G4 with Software 505 + Roche insulin pump</td>
<td>Dexcom G4 Platinum + two Tandem t:slim insulin pumps</td>
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</tr>
<tr>
<td><strong>Time within range 70-180 mg/dl</strong></td>
<td>72%</td>
<td>77%</td>
<td>78%</td>
</tr>
<tr>
<td><strong>Insulin injection U/kg/day</strong></td>
<td>0.66</td>
<td>0.57</td>
<td>0.66</td>
</tr>
<tr>
<td><strong>Glucagon injection</strong></td>
<td>none</td>
<td>none</td>
<td>0.51 mg/day</td>
</tr>
<tr>
<td><strong>Time below 70 mg/dl</strong></td>
<td>2.9%</td>
<td>1.3%</td>
<td>1.8%</td>
</tr>
<tr>
<td></td>
<td>(42 minutes/day)</td>
<td>(19 minutes/day)</td>
<td>(26 minutes/day)</td>
</tr>
<tr>
<td><strong>Time below 60 mg/dl</strong></td>
<td>-</td>
<td>0.3%</td>
<td>0.6%</td>
</tr>
<tr>
<td><strong>Time below 50 mg/dl</strong></td>
<td>0.4%</td>
<td>0.1%</td>
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<td>PID with insulin feedback</td>
<td>Model-based sliding target</td>
<td>-</td>
</tr>
<tr>
<td>Time within range 70-180 mg/dl</td>
<td>72%</td>
<td>77%</td>
<td>78%</td>
</tr>
<tr>
<td>Insulin injection U/kg/day</td>
<td>0.66</td>
<td>0.57</td>
<td>0.66</td>
</tr>
<tr>
<td>Glucagon injection</td>
<td>none</td>
<td>none</td>
<td>0.51 mg/day</td>
</tr>
<tr>
<td>Time below 70 mg/dl</td>
<td><strong>2.9%</strong> (42 minutes/day)</td>
<td><strong>1.3%</strong> (19 minutes/day)</td>
<td><strong>1.8%</strong> (26 minutes/day)</td>
</tr>
<tr>
<td>Time below 60 mg/dl</td>
<td>-</td>
<td>0.3%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Time below 50 mg/dl</td>
<td>0.4%</td>
<td>0.1%</td>
<td>0.1%</td>
</tr>
</tbody>
</table>
Overall AP Challenges

1. CGM accuracy (e.g. at extremes), failure
2. Too Many Delays

Cobelli et al, Diabetes 2011
Overall AP Challenges

1. CGM accuracy (e.g. at extremes), failure
2. Too Many Delays
3. Complexity/connectivity of devices

Algorithmic Solutions:

- Can be modeled into the algorithm
- Detection of sensor failures
- Revert to Open Loop mode with system failure
AP Timeline

“Within about...”

Steps:
- Definitive safety
- Establishment of “final” system
- Industry agreements
- FDA approval

Speedier timing:
- European approval
- Approval of AP technologies besides closed-loop

Web-based remote monitoring/alert system
Lingering Questions

Will adolescents be willing to increase their diabetes-related effort for the gain of automated insulin delivery?

Will well-controlled individuals start unhealthy practices, expecting the system to compensate?
Bridging the canyon...
Bridging the canyon...

“\textquote[I want my old pancreas back!]}{X}

- No worry about hypo’s. \textquote[X]
- Food flexibility. \textquote[+/-]
- No blood sugar checking. \textquote[X]
- Sports without distraction. \textquote[+/-]
- A good night’s sleep. \textquote[✔]
Bridging the canyon...
Bridging the canyon...

Real  Ideal
Bridging the canyon...