Current and Future CGM Technology

Tomas C. Walker, DNP, APRN, CDE
Director, Clinical Projects
Dexcom, Inc
San Diego, CA

Objectives
1. Review past and present CGM technologies.
2. Understand the current and future focus on sharing data.
3. Discuss the future of CGM.

Diabetes in the U.S. in 2012
• 29.1 million individuals with diabetes (~9.1%)  
  – Only ~30% of those are appropriately treated  
  – Less than 10% are under specialty care  
• Incidence of T1 DM climbing at 2-3%/yr  
• Cost exceeds $245 Billion in direct and indirect expenditure  
  – What percentage $ is spent on clinical care?
• What’s the average A1c for a person with T1DM in the US?

So What happened with HbA1c?

SMBG is the Standard of Care
BUT...
  – Misses highs & lows  
  – Accuracy can be problematic  
  – No information on rate/direction of change/or recent past  
  – Only as good as often as you test

So for 35 + years....
• Managing DM was a roller coaster  
  – You poked  
  – You tested  
  – You made your best guess...  
• Sometimes you hit it right..sometimes not
Which Brings us to the Search for a Solution…

- Wouldn’t it be better to monitor the glucose continuously?
- Wouldn’t it be better to ALWAYS know what the sugar is doing?
- Yes, that would be better…that would be Continuous Glucose Monitoring…

1967 The Enzyme Electrode

2001 Cygnus Glucowatch (GW)

- First FDA approved real time device (2001)
- MARD 24.5%
- Reverse iontophoresis
- Through intact skin
- Significant Limitations
- Poor performance
- 13h duration
- High hassle factor
- Skin irritation
- Discomfort limited use

2006 The Year EVERYTHING Changed

Dexcom STS 3 day

And the experimenting started

Mighty Cherry Charger Jamba Juice

- Dexcom
- Ultra

Ate 100gm carbs

2006 Borrowed w/Permission from M.Vogel, www.insulinfactor.com
Continuous Advances in Accuracy

![Accuracy (Mean ARD) for Dexcom Product Generations](chart)

### JDRF Study: The problem wasn’t adults vs. kids, but sustained users vs. not (≥ 6 days/week)

![Change in A1C](chart)

### Patient perception of CGM accuracy is important

- **Low accuracy- Burden**
  - Undermines patient confidence in CGM and CGM data
  - Intermittent or no use
  - Reduced clinical benefit
  - Nuisance alarms ("alarm fatigue")
- **High accuracy- Benefit**
  - Builds patient confidence in CGM and CGM data
  - Regular use (≥ 6 days/week)
  - Improved outcomes: both clinical (≥ 0.5% reduction in A1C) and QoL

### The Role of “Sensor Algorithms” in the Operation and Performance of CGM Devices

- Glucose oxidase reaction
  - Current signal
  - AD converter measures signal
- Need for sensor algorithms
  - Convert sensor count to glucose values
  - Compensate for errors in raw sensor signal
- Additional algorithms
  - "smooth data"
  - May improve accuracy
  - May also increase apparent lag time

\[ y = mx + b \]

### Software 505 is a Further Advancement

<table>
<thead>
<tr>
<th>Study</th>
<th>Day 1</th>
<th>Day 1, 7</th>
<th>Day 2, 20</th>
<th>Day 1, 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>G4 PLATINUM Pivotal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>4524</td>
<td>4524</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAD %20</td>
<td>16.8</td>
<td>16.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%20/20</td>
<td>70.8</td>
<td>70.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G4 with SW 505 Pivotal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>773</td>
<td>773</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAD %20</td>
<td>10.7</td>
<td>10.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%20/20</td>
<td>84.4</td>
<td>84.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G4 PLATINUM and G4 PLATINUM with SW 505 Accuracy versus YSI by In-Clinic Day over the Glucose Range 40-400 mg/dl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Day 1</td>
<td>Day 1, 7</td>
<td>Day 2, 20</td>
<td>Day 1, 20</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-------</td>
<td>----------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>G4 PLATINUM Pivotal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>624</td>
<td>624</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAD %20</td>
<td>11.8</td>
<td>11.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%20/20</td>
<td>82.1</td>
<td>82.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G4 with SW 505 Pivotal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>110</td>
<td>110</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAD %20</td>
<td>6.4</td>
<td>6.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>%20/20</td>
<td>96.4</td>
<td>96.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SW 505 Results from Pediatric Study

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>MARD %</th>
<th>%20/20</th>
</tr>
</thead>
<tbody>
<tr>
<td>G4 PLATINUM with SW 505 Adults</td>
<td>2263</td>
<td>9</td>
<td>93</td>
</tr>
<tr>
<td>G4 PLATINUM with SW 505 Pediatrics</td>
<td>2262</td>
<td>10</td>
<td>91</td>
</tr>
</tbody>
</table>

- During the youth’s participation in the clinic session, G4 PLATINUM with Software 505 detected 91% (225/247) of low (≤ 80 mg/dL) YSI readings within 15 mins.
- 97% (1038/1070) of high (≥ 200 mg/dL) YSI readings within 15 mins.

Laffel et al. “Performance of a New Continuous Glucose Monitoring System (CGM) in Youth” AFDD 2003

What about SHARING data:

- Can Remote Monitoring make a difference?
  - “Remote monitoring significantly decreased prolonged hypoglycemic events, eliminating all events <50 mg/dL lasting longer than 30 min as well as all events <70 mg/dL lasting more than 2 hours.”

DeSalvo et al. “Remote glucose monitoring in camp setting reduces the risk of prolonged nocturnal hypoglycemia” Diabetes Technology and Therapeutics, 2014 Jan;16(1):1-7

Dexcom SHARE

The SHARE APP → CLOUD → FOLLOW APP

Dexcom SHARE APP

SHARER Can Decide:
- What to SHARE
- When to SHARE
- Can Set threshold
- Alerts that are different from the follower

Allows a different SHARE profile for each FOLLOWER
**Dexcom Follow App**

- Allows caregivers to receive notifications of glucose excursions
- Allows caregivers to view glucose trends on demand
- The combination of cloud computing and smartphone technology allows for significant flexibility

**Share & Follow Features**

- Share with up to 5 followers
  - Have to be invited
  - Can select what data to share and when
- Follow up to 5 Sharers
  - Select Alarms for each one you follow
  - Look at their data when convenient
- Securely Transmit Glucose Data
- Share / Follow require an iOS device and wifi or cellular data services

**Android Follow**

**Continuous Integration**

**Dexcom G5 Mobile**

**User Experience**

The user experience for CGM customers is redefined with an improved & intuitive user interface, and a cell phone 'receiver' bridging the gap between medical devices and consumer electronics.

**Dexcom G5 Mobile**

- Same Sensor (G4 Platinum)
- G4AP Algorithm (Software 505)
- New Bluetooth Smart Transmitter
- CGM App
**In App Help Screens**

**Dexcom G5 Mobile with built in Share**

Securely SHARE your Glucose data with up to 5 followers!

**Dexcom G5 Mobile**

**Apple Watch and Follow APP**

**New Sensor Applicator and Wearable**

- Automatic Applicator
  - Improved ease of use
- Low Profile Smart Transmitter
  - 30% smaller than G4 wearable with slim transmitter

**Single Handed Use**
Dexcom’s Next Generation Sensor

- Reduced calibrations leading to factory calibration
- Maintain high level of accuracy
- No signal response to Acetaminophen
- Extended duration

Next generation sensor: Eliminate fingersticks and extend wear

- Single center trial (n=1 site)
- n=40 Type I adult subjects
- Sensors inserted in abdomen
- Two week sensor wear
- Calibrated using 2 SMBG points entered after 2 hour sensor warm-up
- CGM systems were blinded
- Analyzed vs. SMBG

<table>
<thead>
<tr>
<th>Days</th>
<th>MARD</th>
<th>%20/20</th>
<th>%40/40</th>
<th>Hypo MAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-7</td>
<td>11.7%</td>
<td>85.6</td>
<td>98.4</td>
<td>9.4 mg/dL</td>
</tr>
<tr>
<td>1-10</td>
<td>12.1%</td>
<td>84.0</td>
<td>98.4</td>
<td>9.7 mg/dL</td>
</tr>
</tbody>
</table>

Pump integration: Current and Future

ANIMAS VIBE
Approved December 2014

Tandem T-Slim with CGM
***NOT FDA APPROVED***
For investigational use only

Ongoing relationships with Insulet (OmniPOD) and Asante SNAP

The Artificial Pancreas

Components of the AP

- Insulin pump
  - Many pumps are currently used in AP projects
- CGMS
  - 19 of 23 current AP projects are based on Dexcom Technologies
- Blood Glucose Meters
  - Accuracy of BG is good – BUT
- Algorithm
  - The crown jewels of every AP program

What will have the biggest impact on AP research in 2015!

- Money
  - $20 Million in NIH Money*
    - To fund 1 – 3 AP groups
    - Goal is a commercialized AP

*NIH Funding opportunity RA/DC-14-024
Biostator, one of the first closed loop systems, 1977

The Artificial Pancreas in 2010

Florence prototype

The DiAs Platform
University of Virginia

The Dual Hormone Bionic Pancreas
Beacon Hill Study

- 5-day experiments in adults with Type 1 Diabetes
  - 20 adults 21 years and older
- Randomized cross-over design
  - 5 days on bionic pancreas
  - 5 days usual care
- Free run of Boston peninsula east of Mass Ave.

Summer Camp Study

- 5-day experiments in adolescents with Type 1 Diabetes
  - 16 boys, 16 girls (12-20 years old)
- Randomized cross-over design
  - 5 days on bionic pancreas
  - 5 days usual care
- Study and camp staff provide 24-hour coverage to monitor glycemia

Study results of Bionic Pancreas at night

<table>
<thead>
<tr>
<th></th>
<th>Adults (Beacon Hill)</th>
<th>Adolescents (Summer Camp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day and Night</td>
<td>Mean CGM: 133 mg/dL</td>
<td>Mean CGM: 142 mg/dL</td>
</tr>
<tr>
<td></td>
<td>1.5% of time &lt; 60 mg/dL</td>
<td>1.3% of time &lt; 60 mg/dL</td>
</tr>
<tr>
<td>Nighttime Only</td>
<td>Mean CGM: 126 mg/dL</td>
<td>Mean CGM: 124 mg/dL</td>
</tr>
<tr>
<td></td>
<td>0.4% of time &lt; 60 mg/dL</td>
<td>1.0% of time &lt; 60 mg/dL</td>
</tr>
</tbody>
</table>

Bionic Pancreas study results

- Multiple home studies on going
  - Planning on further evaluation of glucagon
- Large scale out patient studies for up to 6 mos being planned

At Home on the UVA Artificial Pancreas

- Day and Night: Mean CGM: 133 mg/dL, 1.5% of time < 60 mg/dL
- Nighttime Only: Mean CGM: 126 mg/dL, 0.4% of time < 60 mg/dL
UVA AP@Home

- More than 100K hours of Closed Loop Data
- Developing a Modular Platform
  - multiple pump support
  - Testing and tuning multiple algorithms
- Single Hormone Approach
  - Integrating consumer electronics and medical devices

At this moment, ~20 people in Europe and in the U.S. are on the DiAs system at home or in hotels as part of three different studies.

AP Outcomes

- The projects are showing
  - Reduced time hypoglycemic
  - Increased “time in range”
  - Improved control overnight
  - Patients are readily adapting to it
  - Excellent safety profiles
  - Technical challenges are being overcome quickly

Challenges for the AP projects

- Battery life
- Constantly advancing products
- Where do you want to put the AP Control
  - In the pump? In the Controller? In the BGM?
- Electronic noise and interference
- Safety/HIPAA/Confidentiality issues
- Should we use Glucagon?
- Best Algorithm for use?
- Will anyone pay for this? Liability issues?

What does the FDA think?

- The FDA sees a pathway ….but….
  - Low Glucose Suspend
  - Hypo & Hyperglycemia minimizers
  - Partially Closed Loop
    - During sleep – meal announcements
  - Full Closed Loop

Other things Dexcom is working on…

- New Sensor and Algorithms to support:
  - Reduced Calibration
  - Interferent blocking
  - Remove Acetaminophen interference
  - Longer sensor life
  - Factory calibration
  - Non-Adjunctive use considerations
  - Smaller Transmitters
  - Smaller Sensors
Take Aways

• CGM technology has made remarkable improvements
  ◦ No comparison between 2006 and today
• Multiple platforms will be supporting integrated pumps and CGM in the near future
  ◦ Smarter pumps are here and more are coming
• Integrating into consumer devices is a priority!
• The Artificial Pancreas is making real progress
  ◦ Many questions still remain

Be part of the journey

THANK YOU! Questions?