Role of CGM for Achieving Glycemic Targets
Howard A. Wolpert, MD
Overview:

- Role of CGM in minimizing hypoglycemia
- Patient specific barriers to use of CGM
- Implication of interstitial vs blood glucose monitoring
- Common pitfalls in CGM use
- Interpreting CGM downloads
- Optimizing alarm settings
Trade-off between Complications & Hypoglycemia

Rate of progression of retinopathy (per 100 patient years)

Rate of severe hypoglycaemia (per 100 patient years)

Severe Hypoglycaemia

Relative risk of Retinopathy

HbA₁c (%)
CGM Features

- More complete picture of glucose patterns than intermittent, capillary blood glucose monitoring
- Glucose trend/rate of change
- Glucose alarms - threshold & predictive
Use of Real-time CGM Reduces Glycemic Variability & Hypoglycemia

Garg, 2006
Use of Real-time CGM Reduces Glycemic Variability & Hypoglycemia

Control (blinded) Group

Display (real-time) Group

Garg, 2006
Changes in HbA1c in ≥25-year olds

RT-CGM

Control

Difference: −0.53%
p value <0.001

JDRF CGM Study Group, 2008
Percent Values ≤50mg/dL (2.8mmol/L)  
Age ≥25 years

JDRF CGM Study Group, 2008
Percent Values ≤50mg/dL (2.8mmol/L)
Age ≥25 years, RT-CGM Group

<table>
<thead>
<tr>
<th>Time</th>
<th>Percent Values</th>
<th>Baseline</th>
<th>26 weeks</th>
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<tr>
<td>Overall</td>
<td>2.2</td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>6am–6pm</td>
<td>3.1</td>
<td>1.6</td>
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<tr>
<td>Noon–6pm</td>
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<tr>
<td>6pm–MN</td>
<td>2.0</td>
<td>0.7</td>
<td>0.7</td>
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</table>
3.0 RT-CGM in Adult Outpatients

Recommendation
3.1 We recommend that RT-CGM devices be used by adult patients with T1DM who have HbA1c levels of at least 7.0% and who have demonstrated they can use these devices on a nearly daily basis (1|★★★★★).
CGM Trade-offs: Benefits vs Hassles

- Frequent hypos or fear of hypoglycemia: benefits outweigh demands
- Technological advances (easy of use, improved accuracy, signal stability): trade-off shifts in favor of benefit > accelerated adoption
- Comparing current CGM devices (Dexcom G4 vs Medtronic Enlite) trade-offs are different
Medtronic Enlite less accurate than Dexcom G4

Performance Comparison of the Medtronic Sof-Sensor and Enlite Glucose Sensors in Inpatient Studies of Individuals with Type 1 Diabetes

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 15, Number 9, 2013

Performance Evaluation of a Continuous Glucose Monitoring System under Conditions Similar to Daily Life

Journal of Diabetes Science and Technology
Volume 7, Issue 4, July 2013

<table>
<thead>
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<th>Number of pairs</th>
<th>RADa</th>
<th>SAR-Sensor</th>
<th>Enlite</th>
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<td>Overall</td>
<td>3,627</td>
<td>1,666</td>
<td>12% (6%, 21%)</td>
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<td>Reference glucose (mg/dL)</td>
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<tr>
<td>≤70</td>
<td>210</td>
<td>122</td>
<td>14% (7%, 38%)</td>
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<td>71–120</td>
<td>1,713</td>
<td>691</td>
<td>13% (6%, 21%)</td>
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<td>121–180</td>
<td>1,086</td>
<td>559</td>
<td>12% (6%, 21%)</td>
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<tr>
<td>&gt;180</td>
<td>618</td>
<td>294</td>
<td>10% (5%, 19%)</td>
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Dexcom G4:
MARD on successive days
CGM Trade-offs: Benefits vs Hassles

- Sensor usage is key predictor of benefit from CGM
- Real-world comparative data on long-term sensor adherence with Dexcom G4 vs Medtronic Enlite are needed for informed clinical decision-making
- RCTs are of little value in predicting real-world sensor usage because of subject selection bias and protocol enforced sensor adherence
Challenges in Sustaining Adherence in the CGM-user

Reducing risk for Sensor Burnout needs to be a major focus in clinical care of the CGM-user

Potential Complications:
- Sensor Burnout:
  - Hardware hassles
  - Information overload
  - Alarm fatigue

Potential Barriers:
- CGM use
Overview:

- Role of CGM in minimizing hypoglycemia
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Common pitfalls in CGM use
Physiologic Delay between Blood and Interstitial Glucose

Current monitors: capillary glucose
Continuous sensors: interstitial glucose

Capillary & interstitial glucose do not always correspond:

- ~ 5+ minute delay in equilibration
- ↑ glucose after meals - capillary before interstitium
- ↓ glucose with insulin & exercise - sometimes interstitium before capillary

From Koschinsky, 2001 (modified after Rebrin, 1999)
Practical Implications of the Physiologic Lag between Blood & Interstitial Glucose:

• Assessment of Device Accuracy
• Calibration of Sensors
• Use of Real Time-CGM in Diabetes Management
• Reliability of Hypoglycemia Alarms
Effect of Increasing Glucose on CGM Accuracy

Point Error-Grid

Relatively stable glucose
Rate: -0.06, 0.06 mmol/l/min

Increasing glucose
Rate: > 0.11 mmol/l/min

Wenthold, 2006
Analytical Accuracy of CGM Deteriorates when Glucose is Changing Rapidly

<table>
<thead>
<tr>
<th>Rate of change (mg/dL/min)</th>
<th>Clark error grid</th>
<th>Median absolute relative difference (%)</th>
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<td>B</td>
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<td>-2 to -1</td>
<td>71.7</td>
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<tr>
<td>-1 to 1</td>
<td>84.9</td>
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<tr>
<td>1 to 2</td>
<td>79.8</td>
<td>18.9</td>
</tr>
<tr>
<td>&gt; 2</td>
<td>63.5</td>
<td>34.7</td>
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Weinstein, 2007
Analytical Accuracy of CGM Deteriorates when Glucose is Changing Rapidly

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<td>0.0</td>
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<td>16.9</td>
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Calibration of Sensor during Non-steady State → Inaccuracy

 Patients should calibrate CGM device during steady state conditions
Physiologic Lag causes CGM to Underestimate Rate of Decline in Glucose

Exercise-induced change (mg/dL/min)

Wilson, 2007
Physiologic Lag affects CGM Readings during Recovery from Hypoglycemia

Use of sensor/interstitial glucose measurements to assess response to treatment of low glucose may lead to over-treatment

Patients should use fingerstick capillary glucose to assess response to treatment of reactions

Cheyne, 2002
29 year old woman with type 1 DM X 20 years
A1c 7.9%, did not change with real-time CGM

Hypoglycemia
- Basal Rate Reduction
- Exaggerated Rebound Hyperglycemia
Teaching Point

In the Pump/CGM-user with marked post-hypoglycemia rebound
Check if the patient is:

- Reducing basal rates when hypoglycemic
- Using CGM to assess response to treatment of hypoglycemia
Overview:

- Role of CGM in minimizing hypoglycemia
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- Common pitfalls in CGM use
- Interpreting CGM downloads
Identifying Glycemic Trouble Spots

Frequent Hyperglycemia

Frequent Hypoglycemia
Identifying Glycemic Trouble Spots

Frequent Hyperglycemia
No Hypoglycemia
Identifying Glycemic Trouble Spots

Frequent Hyperglycemia
High Variability
Limitations of CGM Alarms: Trade-off between Sensitivity & Specificity

Modeling analysis based on:
glucose decline at 1 mg/dL/min & 5 min sampling frequency

Clinical challenge in setting alarm thresholds:
Derive benefit from CGM alarms....
but minimize alarm fatigue

Noujaim, 2007
An Approach to CGM Alarm Optimization

Setting alarm thresholds on the sensor are like setting basal rates on the pump

Initial Step

Considerations in setting initial alarm settings at CGM start

Follow up Step(s)

Review CGM tracings over time to optimize alarm settings
Setting Initial Alarm Thresholds

**Initial Step**

Hx of Severe Hypoglycemia or Hypo Unawareness:

- LO threshold at 80 mg/dL or even higher

Low alarm will warn of most hypos
Benefit outweighs frequent false alarms
Setting Initial Alarm Thresholds

Initial Step

For many individuals:

- LO threshold at 55-60 mg/dL,
  HI threshold at 250 mg/dL or even higher

While getting used to the sensor & smoothing out glucose patterns:
- Less intrusive/irritating alarms
- Less risk for alarm burnout
Using CGM Data to Optimize Alarm Settings

Initial Step

Follow up Step(s)

Retrospective review of CGM tracings:

- Did the alarm alert the patient of all low & high gluoses? 
- Did the patient hear/feel the alarm when the tracing indicates that the glucose went below the LO threshold & above the HI threshold? 
- How many false alarms is the patient experiencing?
Using CGM Data to Optimize Alarm Settings

Retrospective review of CGM tracings:

If fasting glucoses often high, but no overnight HI alarm
→ Check whether patient hears/feels the alarm
→ Decrease the HI alarm threshold

If the HI alarm is going off:
- Too often
- Frequently when glucose is not, in fact, high
→ Increase the HI alarm threshold or snooze duration
Major consideration in setting HI alarm:
Frequent fasting hyperglycemia due to variable overnight control

HI alarm threshold set at 280 mg/dL
Major consideration in setting HI alarm: Frequent fasting hyperglycemia due to variable overnight control
Glucose will take several hours to decline following correction bolus → snooze function reduces “nuisance” alarms
Retrospective review of CGM tracings:

If frequent hypos, but no LO alarm
→ Check whether patient hears/feels the alarm
→ Increase the LO alarm threshold

If the LO alarm is going off:
- Too often
- Frequently when, in fact, not hypo
→ Decrease the LO alarm threshold
Sensor Lag can reduce alarm accuracy: a consideration in setting alarm thresholds.

Alarm thresholds:
- HI 200
- LO 60

Sensor G = 200
Fingerstick G = 238

Correction bolus

Wakes up:
- Fingerstick G = 52, but Sensor G > 70 so Alarm did not sound

Recommendation:
Increase LO alarm threshold to 70-75
Technology is a tool for enhanced diabetes self-management: the outcome is user-dependent

Important considerations to enhance benefit:

- Patient specific barriers to use of CGM
- Implication of interstitial vs blood glucose monitoring
  Common pitfalls in CGM use
- Optimizing alarm settings
Thank you