Real-Time Continuous Glucose Monitoring: From Application to Evaluation

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Why CGM?

• HbA1c levels still fall far short of target in the majority of patients
• Quality of life must be taken into account
  – Severe hypoglycemia remains a major risk for insulin users
  – Acute hyperglycemia has an impact on emotions, mental and intellectual abilities, and physical performance

Proven Need

30 children wearing a CGM device for 3 months*

<table>
<thead>
<tr>
<th>Glucose Threshold</th>
<th>Average Hours Each Day Above Threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.0 mmol</td>
<td>8.7</td>
</tr>
<tr>
<td>11.1 mmol</td>
<td>6.6</td>
</tr>
<tr>
<td>13.9 mmol</td>
<td>2.8</td>
</tr>
<tr>
<td>16.7 mmol</td>
<td>0.9</td>
</tr>
</tbody>
</table>


How It Works

• Glucose sensor is inserted in subcutaneous tissue and connected to a transmitter
• Glucose sensor sends minute electrical signals to the transmitter
• Transmitter sends data wirelessly to a pump or handheld monitor, where data can be viewed and acted upon in real-time

Proven Need

30 children wearing a CGM device for 3 months*

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<th>Glucose Threshold</th>
<th>Average Minutes Each Day Below Threshold</th>
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<tr>
<td>3.9 mmol</td>
<td>71</td>
</tr>
<tr>
<td>3.3 mmol</td>
<td>34</td>
</tr>
<tr>
<td>2.8 mmol</td>
<td>14</td>
</tr>
<tr>
<td>2.2 mmol</td>
<td>5</td>
</tr>
</tbody>
</table>


How It Works

Glucose Oxidase enzyme

Glucose + O₂ → H₂O₂ + Gluconic Acid

H₂O₂ → 2H⁺ + O₂ + 2 e⁻
How It Works

System Performance
- Sensors generally last 5-14 days*
- Warm-up period after insertion; calibration
- Accuracy
  - Clarke error grid: 98%+ in zones A & B (low risk of accidental insulin overdose)
  - Mean absolute difference (real-time CGM vs SMBG): ~15%

System Options
- MiniMed Paradigm® REAL-Time Insulin Pump and Continuous Glucose Monitoring System*
- Guardian® REAL-Time Continuous Glucose Monitoring System*
- DexCom™ STS®
- Medtronic iPro® Recorder
- Freestyle Navigator™

* On-label information

CGM Options

FDA Approved
- GlucoWatch® G2™ Biographer¹
- CGMS® System Gold™²
- MiniMed Paradigm® REAL-Time Insulin Pump and Continuous Glucose Monitoring System²
- Guardian® REAL-Time Continuous Glucose Monitoring System²
- DexCom™ STS³
- DexCom™ STS-7⁴
- Medtronic iPro® Recorder
- Freestyle Navigator™⁴


MiniMed Paradigm® & Guardian® REAL-Time CGM Systems

On-Screen Reports
- 3-hr and 24-hr graphs (pump); 3 / 6 / 12 / 24-hr graphs (guardian)
- Can scroll back for specific data points
- “direction” indicators
- Updates every 5 minutes
- Sensor change/restart after 3 days
- 2-3 calibrations/day

Medtronic Paradigm® & Guardian® REAL-Time CGM Systems

Real Time and Retrospective

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
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</thead>
<tbody>
<tr>
<td>Predictive Alerts (Guardian)</td>
<td>Relatively Short sensor life</td>
</tr>
<tr>
<td>3, 6, 12 &amp; 24-hr graphs, plus datapoint history on screen</td>
<td>Transmitter must be charged</td>
</tr>
<tr>
<td>Customizable alerts, Predictive alerts (Guardian)</td>
<td>Expensive to replace transmitters</td>
</tr>
<tr>
<td>Uploadable to Carelink web site for analysis</td>
<td>Cannot use “Link” Meter when sensor is used</td>
</tr>
<tr>
<td>No need for extra monitor (if using latest pump)</td>
<td>Alarms may go unnoticed</td>
</tr>
<tr>
<td>Memory chip in transmitter stores data when monitor out of range</td>
<td>Worst accuracy of available systems</td>
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</table>
**MiniMed Paradigm® & Guardian® REAL-Time CGM Systems**

**CareLink™ Personal:**

**12 Report Options**

- Pump settings
- Insulin delivery
- Blood glucose data
- Sensor glucose data
- Carbohydrate & logbook entries
- Can sort by time frame
- PDF reports can be viewed online, saved, printed, and e-mailed

**MiniMed Paradigm® & Guardian® REAL-Time CGM Systems**

**CareLink™ Personal:**

**Key Reports**

- Sensor daily overlay
- Sensor overlay by meal

**DexCom™ 7 STS®**

**Reports**

- Hourly Stats
- Glucose Trend

**System Options**

- 2-hour warmup
- 1, 3, 9-hr graphs
- Updates every 5 minutes
- Sensor change (or restart) after 7 days
- 2-3 calibrations/day

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**DexCom™ 7 STS®**

**Real Time and Retrospective**

<table>
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<th>Pros</th>
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<tr>
<td>Longest-lasting sensors</td>
<td>Limited customization</td>
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<tr>
<td>Self-adhering sensors, strong adhesive</td>
<td>Cumbersome calibration process (older systems)</td>
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<td>Lowest start-up cost</td>
<td>1-hr, 3-hr, and 9-hr graphs only</td>
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<tr>
<td>Company willing to replace lost parts, nonproductive sensors</td>
<td>Cursory analysis software</td>
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<td>Very loud alarm</td>
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<td>Limited insurance support</td>
<td>Acetaminophin Effect</td>
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**DexCom™ 7 STS®**

**Real Time and Retrospective**

**Pros**

- Longest-lasting sensors
- Self-adhering sensors, strong adhesive
- Lowest start-up cost
- Company willing to replace lost parts, nonproductive sensors
- Very loud alarm

**Cons**

- Limited customization
- Cumbersome calibration process (older systems)
- 1-hr, 3-hr, and 9-hr graphs only
- Cursory analysis software
- Very loud alarm
- Limited insurance support
- Acetaminophin Effect
**DexCom™ 7 STS®**

**Reports**
- BG Distribution
- Trend Analysis

**Freestyle Navigator™**

**Real Time and Retrospective**
- 2 / 4 / 6 / 12 / 24-hr graphs
- Predictive alarms
- “direction” indicators
- Updates every minute
- Sensor change/restart after 5 days
- <1 calibration/day

**Pros**
- Best accuracy of RT systems
- BG meter built into monitor
- Detailed on-screen data analysis
- Extensive customization options, predictive alerts
- Fewest calibrations required
- Aggressive insurance dept.
- Widest transmitter range

**Cons**
- 10-hr warm-up period
- Large transmitter
- Costliest system & sensors
- Must calibrate w/Freestyle meter

**Drawbacks & Limitations to Real-Time CGM**
- Cost of monitors, transmitters & sensors
- False alarms
- Inaccuracy (encapsulation tissue, lag time)
- False sense of security (false negatives)
- Pincushion effect, Extra "equipment"
- User maintenance

**Interstitial Fluid and “Lag Time”**
- Capillary glucose must diffuse into the interstitial fluid (ISF)
- ISF glucose levels may lag capillary levels by 5–15 minutes
- When glucose levels are stable, ISF glucose levels and capillary blood glucose levels are similar


**Encapsulation Tissue**
- Anything implanted in the body becomes covered with a protein / collagen layer
- Encapsulation tissue chemically isolates foreign objects, which may be perceived as harmful
- This chemical isolation decreases the sensitivity and longevity of electrochemical sensors
Practical Benefits of Real-Time CGM

- Rumble strips (avoid serious extremes)
- Peace of mind
- Basal & bolus fine tuning
- Postprandial analysis
- Insulin action curve determination
- Short-term Forecasting
- Learning tool & immediate feedback
- Eliminates some blood glucose checks???

Proven Benefit

Reduction in HbA1c with CGM

- CGM vs. SMBG for 3 months
- Both groups received intensive treatment
- Adjustments to therapy were made as required


GuardControl Study

- 162 children (n = 81) and adults (n = 81) with elevated HbA1c using pumps or MDI
- Randomized to continuous use of a CGM device, use 3 days biweekly, or no use (control)
- No differences in insulin usage


Proven Benefit

Reduction in hypoglycemic excursions

- Duration of Hypoglycemic Excursions (minutes per event)


How to Look at the Information

- Immediate
- Intermediate
- Retrospective

Immediate Info: Alarms

- Alarms are designed to alert the patient to interstitial glucose levels that have crossed specified thresholds, either high or low
- They may be vibrating or audible
Setting Alarms

- Alarms should be individually set
- Alarm thresholds are not targets
- Alarms should be set so they balance the need to alert the patient without becoming a nuisance

“Starting Alert Setting”
Recommendation
LOW: 4.5 mmol
HIGH: 13 mmol

NOT RECOMMENDED: Low 4 mmol
NOT RECOMMENDED: High 8 mmol

Special Alarm Settings

- Hypoglycemic unawareness
- Pregnancy
- HbA1c of 11.0%

Immediate Info:
Real-Time Data

- Safety Value
- Prediction/Forecasting
- Replace Fingersticks?
  - After 1st 12-24 hrs
  - BG Stable
  - Recent calibrations in-line
  - No recent system alarms

Immediate Info:
Directional Bolus Adjustment

- BG Stable: Usual Dose
- BG Rising Slowly: ↑ bolus 10%
- BG Rising Quickly: ↑ bolus 20%
- BG Dropping Slowly: ↓ bolus 10%
- BG Dropping Quickly: ↓ bolus 20%

Use of 2/3/4 Hr Graphs

- Food Effects
- Bolus Effectiveness
- Pramlintide/Exenatide Influence
- Exercise Effects
- Impact of Stress
Use of 9 / 12 / 24 Hr Graphs

- Facilitates decision-making for basal insulin doses
- Shows delayed effects of exercise, stress, high-fat foods
- Reveals overnight patterns
- Comparison of school/work vs off days

Specific Insights to Derive
(a purely retrospective journey)

Case Study 1a: Effectiveness of Current Program
- Type 1 diabetes; using insulin glargine & MDI
- Overnight readings are OK; HbA1c levels are elevated
- Meal doses insufficient; not covering snacks?

Case Study 1b: Effectiveness of Current Program
- Type 2 diabetes; taking metformin
- Fasting BG levels generally near 100 mg/dL
- Daytime medication, diet & exercise education needed

Case Study 2a: Basal Insulin Regulation
- Stable 12 AM – 4 AM, then dropping pre-dawn
- Dropping late afternoon

Case Study 2b: Basal Insulin Regulation
- Type 1 diabetes; using insulin glargine & MDI
- History of morning lows
- Now not “covering” highs at night
- BG dropping overnight; insulin dose too high
Case Study 3: Detection of Silent Hypoglycemia
- Type 1 diabetes; on pump
- Frequent fasting highs (9 AM)

Case Study 4: Determination of Insulin Action Curve

Case Study 5: Fine-Tuning Meal Boluses
- Breakfast and lunch doses may be too low
- Dinner dose appears OK
- Night-snack dose clearly insufficient

Case Study 6: Fine-Tuning Correction Boluses
- Dropping low after correcting for highs at bedtime and wake-up time

Case Study 7: Postprandial Analysis
- Pre-meal BG levels are usually in target range
- HbA1c are higher than expected based on SMBG
- Tired and lethargic after meals

Case Study 8: Impact of Physical Activity
- Type 1 diabetes; pump user
- Basal rates confirmed overnight
- Exercises in the evening (9 PM)
Case Study 9: Impact of Stress

• Type 1 diabetes; pump user
• 40 years old; athletic
• Handsome, excellent speaker
• Late for meeting
• Gets flat tire; eats 15g carbs to prepare for tire change
• Spare is flat too!!

STRESS RAISES BLOOD GLUCOSE!!!
Financial
• Insurance letters; building a case
• Appeal, Appeal, Appeal
• Out-of-pocket costs
• Use billing code 95250

To CGM or Not to CGM: The Deciding Factor

**Benefits > Drawbacks**

???