The Utility of Simultaneous Glucose Sensor Measurements

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Clinical glycemic management for a 63 y.o. white male with type 2 diabetes undergoing an esophagectomy (subject D2)
# In-hospital Glycemic Management

| 1-2 hours | Average time between blood glucose tests |
| ~5 minutes | Average time to obtain blood glucose reading with conventional point-of-care device† |
| 4-8% | Percentage of time per patient a nurse must devote to frequent blood glucose monitoring |
| 2:1 (4:1) | Ratio of patient to nurse in ICU (general floor) |

CGM in the Hospital

• Rationale
  – Improve glycemic management
  – Avoid hypoglycemia
  – Reduce workload and cost

• Requirements
  – Accurate
  – Reliable
  – User-friendly
In-hospital CGM Evaluation

- Assessment of two glucose-sensing technologies
  - Interstitial fluid glucose sensors (TGMS)
  - Intravenous glucose sensor (VGMS)

Data collected under the project entitled “Artificial Pancreas for Control of BG and Insulin Levels in Hospitalized Patients with Diabetes and Stress Hyperglycemia” sponsored by the Technologies in Metabolic Monitoring (TMM) Initiative with additional support from Medtronic Diabetes
In-hospital CGM Evaluation

• 10 patients studied in the perioperative period
• Each patient studied for a maximum of 60 hours

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Sex</th>
<th>Age</th>
<th>BMI</th>
<th>C-Peptide*</th>
<th>HbA1c†</th>
<th>Procedure</th>
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<tbody>
<tr>
<td>A3</td>
<td>F</td>
<td>47</td>
<td>19.1</td>
<td>0.7</td>
<td>6.1</td>
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</tr>
<tr>
<td>B3</td>
<td>M</td>
<td>55</td>
<td>22.7</td>
<td>0.8</td>
<td>5.3</td>
<td>whipple procedure</td>
</tr>
<tr>
<td>C3</td>
<td>M</td>
<td>58</td>
<td>22.9</td>
<td>2.1</td>
<td>6.1</td>
<td>whipple procedure</td>
</tr>
<tr>
<td>D3</td>
<td>M</td>
<td>59</td>
<td>29.5</td>
<td>1.0</td>
<td>5.6</td>
<td>whipple procedure</td>
</tr>
<tr>
<td>E3</td>
<td>F</td>
<td>51</td>
<td>20.7</td>
<td>1.2</td>
<td>5.5</td>
<td>whipple procedure</td>
</tr>
<tr>
<td>F3</td>
<td>M</td>
<td>56</td>
<td>27.8</td>
<td>0.8</td>
<td>5.0‡</td>
<td>whipple procedure</td>
</tr>
</tbody>
</table>

T2DM

* reported normal range is 0.8-3.5ng/ml unless otherwise noted
# reported normal range is 0.8-3.1ng/ml
† reported normal range is 3.6-6.9% unless otherwise noted
‡ reported normal range is 4-6%

whipple procedure

panniculectomy and exploratory laparotomy

pancreatic resection cancelled due to metastatic cancer
hepatic resection cancelled due to metastatic cancer
transhiatal esophagectomy
Reference Data

- Arterial (q20 min) and venous (q60 min) glucose, lactate, blood gases and electrolytes levels
- Capillary blood glucose levels (q3 hr)
- Arterial insulin and fatty acids levels
- Urine analysis every hour
- Recorded vital signs, IV infusion rates, body position, sedation, meals and medications
TGMS Sensors

- Guardian RT® sensors (Medtronic Diabetes, Northridge, CA)
- Grouped into two three-sensor arrays
- Inserted into the arm, chest or thigh
- Modified transmitters wirelessly transmit every minute
Sensor/Reference Data

Arterial (red circle) and venous (blue squares) reference glucose measurements (in mg/dl).

TGMS glucose sensor signals (in nA) smoothed with a 7th order FIR filter (sensors 1-6 are red, yellow, green, cyan, blue and magenta, respectively).

Data from subject D2
The mean absolute relative difference (MARD) and Pearson Correlation Coefficient (R) were calculated from paired reference/sensor values. Statistics were computed separately for arterial and venous reference measurements. Sensor data were smoothed using a 7th order FIR filter and recalibrated every six hours using a one-point calibration with a fixed offset after a two-hour run-in period.

*Not pictured: arterial and venous outlying MARD values for subject D3, sensor 1 (1.29 and 2.27) and sensor 3 (3.17 and 1.39)
Sensor Combination Schemes

• Mean
  – Average all six sensor values

• Trimmed Mean
  – Rank the six sensor values and average the second, third, forth and fifth ranked values

• Median
  – Rank the six sensor values and average the third and forth ranked values
Combined Sensor Performance

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Reference</th>
<th>Individual Sensor</th>
<th>Combined Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>median (range)</td>
<td>Mean</td>
</tr>
<tr>
<td>arterial</td>
<td>venous</td>
<td>0.16 (0.08 - 0.34)</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.26 (0.16 - 0.85)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

Combined sensor measures (mean, trimmed mean and median) are displayed in red, green and blue.

Data from subject D2
Combined Sensor Performance

*Not pictured: arterial MARD values for subject D3, sensor 1 and sensor 3 (1.29 and 3.17)

<table>
<thead>
<tr>
<th>Subject</th>
<th>Individual Sensors</th>
<th>Combined Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2</td>
<td>0.11 (0.09 - 0.15)</td>
<td>0.11</td>
</tr>
<tr>
<td>B2</td>
<td>0.18 (0.10 - 0.47)</td>
<td>0.11</td>
</tr>
<tr>
<td>C2</td>
<td>0.29 (0.20 - 0.49)</td>
<td>0.30</td>
</tr>
<tr>
<td>D2</td>
<td>0.16 (0.08 - 0.34)</td>
<td>0.09</td>
</tr>
<tr>
<td>A3</td>
<td>0.15 (0.14 - 0.20)</td>
<td>0.12</td>
</tr>
<tr>
<td>B3</td>
<td>0.17 (0.16 - 0.21)</td>
<td>0.17</td>
</tr>
<tr>
<td>C3</td>
<td>0.13 (0.10 - 0.83)</td>
<td>0.12</td>
</tr>
<tr>
<td>D3</td>
<td>0.39 (0.13 - 3.17)</td>
<td>0.18</td>
</tr>
<tr>
<td>E3</td>
<td>0.26 (0.09 - 0.51)</td>
<td>0.22</td>
</tr>
<tr>
<td>F3</td>
<td>0.14 (0.10 - 0.44)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

MeanTrimmed MeanMedianmedian (range)
Combined Sensor Performance

*Not pictured: venous MARD values for subject D3, sensor 1 and sensor 3 (2.27 and 1.39)

†Insufficient venous reference glucose measurements to complete analysis

<table>
<thead>
<tr>
<th>Subject</th>
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<tr>
<td></td>
<td>median (range)</td>
<td>Mean</td>
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<td>Trimmed Mean</td>
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<tr>
<td></td>
<td>mean (range)</td>
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<tr>
<td>A2</td>
<td>0.19 (0.16 - 0.20)</td>
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<tr>
<td>B2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D2</td>
<td>0.25 (0.16 - 0.85)</td>
<td>0.25</td>
</tr>
<tr>
<td>A3</td>
<td>0.17 (0.15 - 0.19)</td>
<td>0.17</td>
</tr>
<tr>
<td>B3</td>
<td>0.16 (0.16 - 0.23)</td>
<td>0.17</td>
</tr>
<tr>
<td>C3</td>
<td>0.13 (0.13 - 0.76)</td>
<td>0.13</td>
</tr>
<tr>
<td>D3</td>
<td>0.28 (0.16 - 2.27)</td>
<td>0.28</td>
</tr>
<tr>
<td>E3</td>
<td>0.29 (0.19 - 0.53)</td>
<td>0.23</td>
</tr>
<tr>
<td>F3</td>
<td>0.19 (0.12 - 0.36)</td>
<td>0.13</td>
</tr>
</tbody>
</table>
Multiple Sensors

- Robust estimate of blood glucose level (accuracy)
- Identify and replace failed sensor without interruption of data (reliability)
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Subject B2