CONTINUOUS NON-INVASIVE GLUCOSE MONITORING BY SENSOR FUSION OF NEAR INFRARED LIGHT AND BIOIMPEDANCE MEASUREMENTS: RESULTS OF A PROOF OF CONCEPT STUDY

MOTIVATION

Continuous glucose monitoring (CGM)

Subcutaneous (SC) CGM:
- Improve the metabolic control in diabetes mellitus type 1 (DM1).
- Avoid hypoglycemas.
- All commercially available systems use enzyme-based amperometric methods.
- Limited sensor lifespan.

Non-invasive CGM:
- Reduce the burden to the patients.
- Substantially longer sensor lifespan.
- Technically challenging.

METHODS

Non-invasive CGM
- BioMKR device (previously called GlucoPred)
- Wearable device, the size of a wristwatch.
- Two measurement technologies:
  - Diffuse reflectance of near infrared (NIR) light (wavelength range 900-1700 nm).
  - Bioelectrical impedance (1-25 MHz).
- NIR and bioimpedance measurements are converted into glucose estimates.
- Sensor fusion algorithm that reduces noise and artefacts.

Results

Study participants
- 12 DM1 patients, 9 complete datasets.
- 18–80 years. Studied at a university hospital research ward.
- Each participant wore 6 BioMKRs symmetrically on the extremities.
- In total, 12 placements were investigated.
- Hyperinsulinemic clamp techniques and varying glucose infusions to achieve five glucose intervals, ranging from hypoglycemia (1.7-2.8 mmol/L) to hyperglycemia (14.0-22.2 mmol/L). Intravenous glucose measured every 5 minutes. 728 reference samples in total.

Data processing
- Cross-validation (NIR and bioimpedance): Data from each sensor was split in four sections. Three sections were used to calibrate the sensor against measured intravenous glucose levels, used by the BioMKR to estimate the glucose levels in the fourth section. The procedure was repeated four times (i.e. with all four sections as the estimation part).
- Sensor fusion: Data from one sensor was used for calibration. Performance was analyzed on the sensor at the contralateral position.

(*) Sensor fusion may look worse compared to NIR and bioimpedance alone, because it is trained and evaluated on different (contralateral) positions, while NIR and bioimpedance are trained and evaluated on different sections of data from the same sensor location (as described in Methods). In other words, sensor fusion was tested on a more challenging task.

Conclusions

- Non-invasive CGM by sensor fusion technology using NIR and bioimpedance is a promising alternative to the current subcutaneous gold standard for CGM.
- The optimal sensor site has yet to be established, but the posterior side of the upper arm is most promising among the tested sites.
- There are still technical challenges to be resolved.

Fig. 1: Glucose estimate example (Sensor fusion) for one patient, using the sensor at the posterior side of the left upper arm.

<table>
<thead>
<tr>
<th>Sensor position</th>
<th>CEG classification N</th>
<th>Samples</th>
<th>CEG classification B</th>
<th>Samples</th>
<th>CEG classification D</th>
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<tr>
<td>Anterior lower arm left</td>
<td>63.2% 28.9% 7.9%</td>
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<td>266</td>
<td>58.1% 37.9% 1.6%</td>
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<td>Anterior lower arm right</td>
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<td>68.1% 29.4% 2.6%</td>
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<tr>
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<td>-</td>
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<td>-</td>
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<td>56.4% 38.5% 4.1%</td>
<td>1.0%</td>
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<tr>
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<td>-</td>
<td>345</td>
<td>55.0% 36.6% 8.4%</td>
<td>-</td>
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<tr>
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<td>49.8% 37.2% 10.5%</td>
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<tr>
<td>Upper calf left</td>
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<td>261</td>
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<tr>
<td>Upper calf right</td>
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