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

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Motivation

Continuous glucose monitoring (CGM)

Subcutaneus (SC) CGM:

- Improve the metabolic control in diabetes mellitus type 1 (DM1).
- Avoid hypoglycemias.
- 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.

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.

Results

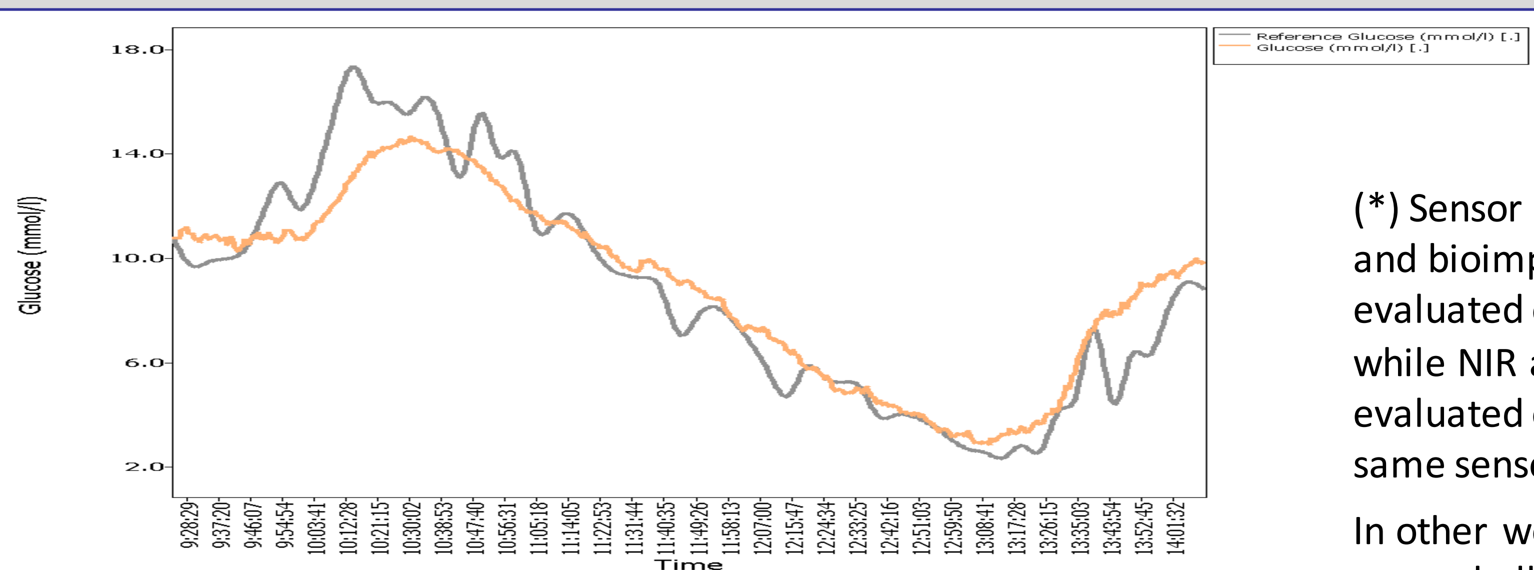

Fig. 1: Glucose estimate example (Sensor fusion) for one patient, using the sensor at the posterior side of the left upper arm.

(*) 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.

	NIR					Bioimpedance					Sensor fusion (*)				
	CEG classification				Samples	CEG classification				Samples	CEG classification				Samples
Sensor position	A	B	C	D	N	A	B	C	D	N	A	B	C	D	N
Anterior lower arm left	63.2 %	28.9 %	7.9 %	-	266	58.1 %	37.9 %	1.6 %	2.4 %	124					
Anterior lower arm right	62.0 %	28.8 %	8.9 %	0.4 %	271	40.7 %	42.6 %	16.7 %	-	54					
Anterior thigh left	72.6 %	22.7 %	4.2 %	0.6 %	361	66.9 %	26.6 %	5.9 %	0.7 %	305	55.8 %	30.8 %	13.5 %	-	52
Anterior thigh right	73.9 %	23.1 %	3.1 %	-	295	70.1 %	23.2 %	6.8 %	-	177					
Anterior upper arm left	71.9 %	22.4 %	5.7 %	-	366	54.1 %	34.0 %	10.6 %	1.3 %	377	47.3 %	42.9 %	4.9 %	4.9 %	182
Anterior upper arm right	83.5 %	15.7 %	0.8 %	-	363	68.1 %	29.4 %	2.6 %	-	235	68.3 %	11.4 %	16.3 %	4.1 %	123
Posterior upper arm left	66.7 %	31.9 %	1.5 %	-	270	52.8 %	36.9 %	10.3 %	-	195	52.6 %	43.9 %	3.5 %	-	114
Posterior upper arm right	76.5 %	22.4 %	1.1 %	-	272	56.4 %	38.5 %	4.1 %	1.0 %	195	65.6 %	21.6 %	12.8 %	-	125
Posterior wrist left	64.9 %	31.0 %	4.1 %	-	345	55.0 %	36.6 %	8.4 %	-	347					
Posterior wrist right	64.6 %	29.1 %	5.0 %	1.3 %	302	49.8 %	37.2 %	10.5 %	2.4 %	247					
Upper calf left	71.6 %	23.0 %	3.8 %	1.5 %	261	55.5 %	36.6 %	7.9 %	-	191					
Upper calf right	67.5 %	30.9 %	1.1 %	0.4 %	265	54.3 %	38.9 %	6.8 %	-	265	68.4 %	18.4 %	13.2 %	-	76
Total	70.3 %	25.5 %	3.9 %	0.3 %	3637	57.6 %	34.2 %	7.5 %	0.7 %	2712	58.5 %	29.6 %	9.8 %	2.1 %	672

Conclusion

- 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.