CGM-based glycemic variability indices allow accurate classification of IGT and T2D subjects

E. Longato[1], G. Acciaroli[1], A. Facchinetti[1], A. Maran[2], G. Sparacino[1], L. Hakaste[3], T. Tuomi[3], and C. Cobelli[1]

[1]Department of Information Engineering, University of Padova, Padova, Italy; [2]Department of Medicine, University of Padova, Padova, Italy;
[3]Folkhälsan Research Centre, Diabetes and Obesity Research Program, University of Helsinki, Helsinki, Finland;

1. INTRODUCTION AND AIM

Tens of glycemic variability (GV) indices are available in the literature. Whether GV indices derived from continuous glucose monitoring (CGM) sensors are effectively usable for classifying patients is, however, still controversial.

Recently, we demonstrated that CGM-based GV indices can be successfully used to distinguish healthy from impaired glucose tolerance (IGT) and type 2 diabetes (T2D) conditions [1].

The aim is to move a step forward with respect to [1] by assessing if a GV-indices based classifier can further distinguish IGT from T2D subjects.

2. DATASET

The dataset consists of 62 subjects extracted from the *Botnia Perspective Study* and the *Botnia PPP Study* [2-4]. Each subject was monitored by either the *Guardian Real Time* or the *iPro* CGM systems (Medtronic, MiniMed, Inc., Northridge, CA) for a few days during 2014 (1st visit) and for a few days during 2015 (2nd visit). According to gold-standard techniques, patients are classified as follows:

- 1st visit: 36 IGT, 26 T2D
- 2nd visit: 37 IGT, 25 T2D (specifically, 2 T2D → IGT, 1 IGT →T2D)

In addition to CGM traces, age, sex, body mass index (BMI) and waist circumference (WC) are also available for each patient.

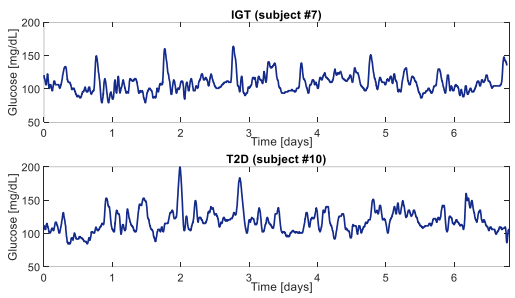

Fig. 1. Representative CGM traces of an IGT (top) and a T2D (bottom).

3. GV INDICES

37 GV indices were extracted from each of the 62 CGM traces:

- Mean
- Median
- Standard deviation (SD)
- Coefficient of variation (CV)
- J-index
- Mean of daily SD
- SD of daily mean
- %values below target
- %values within target
- %values above target
- Mean amplitude of glycemic excursions (MAGE)
- MAGE +
- MAGE -
- M-value
- Moment invariant indices
- Glycemic risk assessment diabetes equation (GRADE)
- GRADE eu
- GRADE hypo
- GRADE hyper
- Hypo index
- Hyper index
- Index of glycemic control (IGC)
- Low blood glucose index (LBGI)
- High blood glucose index (HBGI)
- Blood glucose risk index (BGRI)
- Average daily risk range (ADRR)
- Continuous overall net glycemic action (CONGA)
- Mean of daily differences (MODD)
- Excursion frequency (EF)

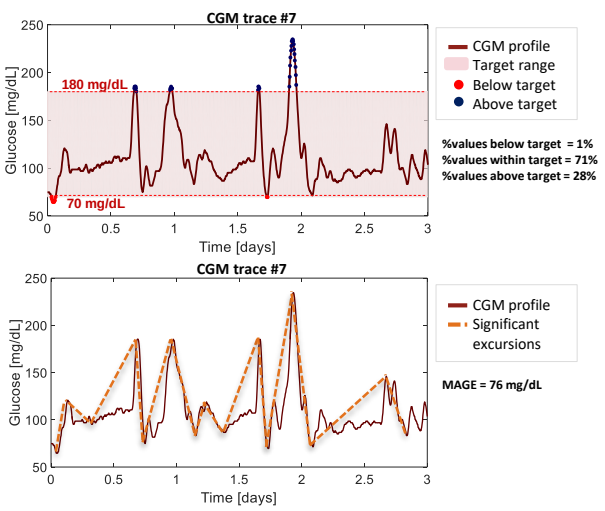

Fig. 2. Examples of 4 GV metrics computed from CGM trace #7. %values below, within and above target range (top) and MAGE (bottom).

4. CLASSIFICATION

To classify each patient we implemented a Support Vector Machine (SVM) classifier with polynomial kernel.

The dataset has been subdivided into training and test sets:

- Training set → first visit (26 IGT, 36 T2D)
- Test set → second visit (25 IGT, 37 T2D)

We tested two different classification scenarios, having the following features as input to the SVM classifier:

- Scenario A → 37 GV indices
- Scenario B → 37 GV indices, as above, plus age, sex, BMI and WC

Classification accuracy is assessed by determining the percentage of subjects in the test group correctly classified.

5. RESULTS

Using GV indices only (scenario A), IGT subjects are distinguished from T2D subjects with 74.2% accuracy. The addition of some basic clinical parameters to GV indices (scenario B) improved this performance to 87.1%.

The confusion matrix of scenario B, which shows the best classification accuracy, is:

TRUE CLASS \ PREDICTED CLASS	IGT	T2D
IGT	31	6
T2D	2	23

Overall, 54 subjects are correctly classified. Only 8 subjects are misclassified: 2 T2D are labeled as IGT and 6 IGT are labeled as T2D.

Classification performance in scenario B is represented in two dimensions via Principal Component Analysis (PCA):

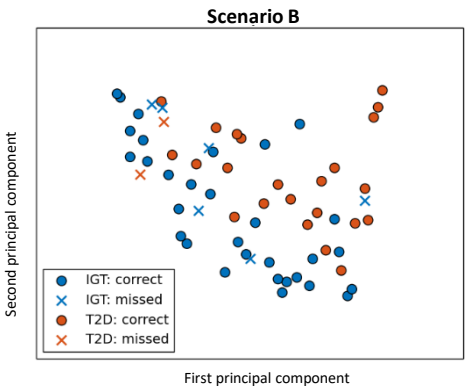

Fig. 3. 2D projection via PCA of classification results obtained through SVM with polynomial kernel in scenario B.

From the 1st to the 2nd visit, two subjects originally classified by gold-standard techniques as T2D switched to IGT condition, whereas one subject deteriorated from IGT to T2D.

Using the SVM classifier in scenario B:

- The IGT subject becoming T2D is correctly detected
- One of the two subjects switching from T2D to IGT is correctly detected

6. CONCLUSIONS

CGM-based GV indices, especially when combined with basic clinical parameters, well behave for distinguishing IGT from T2D subjects.

Further work will concern the extension of the database and the identification of the minimal set of GV indices needed for classification purposes.

REFERENCES:

[1] Acciaroli et al., "Good accuracy of CGM-based glucose variability indices for IGT and T2D classification," *16th Annual Diabetes Technology Meeting*, 2016.
[2] Groop et al., "Metabolic consequences of a family history of NIDDM (the Botnia study): evidence for sex-specific parental effects," *Diabetes, 1996.*
[3] Pyykkonen et al., "Stressful life events and the metabolic syndrome: the prevalence, prediction and prevention of diabetes (PPP)-Botnia Study," *Diabetes Care*, 2010.
[4] Almgren et al., "Heritability and familiality of type 2 diabetes and related quantitative traits in the Botnia Study," *Diabetologia*, 2011.

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CONTACT: Giada Acciaroli, giada.acciaroli@phd.unipd.it