Experiment Protocol of the Project Non-invasive Blood Glucose Measurement using Photoplethysmography and AI Machine Learning Algorithm

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1 Introduction

Diabetes is a chronic disease that affects more than 400 million people worldwide, according to the World Health Organization. The blood glucose meter market is expected to grow from USD 7,419.0 Million in 2018 to USD 15,415.6 Million by 2026, with a compound annual growth rate (CAGR) of 9.6% [2]. However, current blood glucose meters rely on invasive blood tests, which may discourage frequent monitoring and fail to provide real-time feedback. Therefore, there is an urgent need for a non-invasive blood glucose monitoring device to enhance diabetes management.

Photoplethysmography (PPG) is a promising technique for non-invasive blood glucose measurement, as it can estimate biological parameters from optical signals and has low cost [4]. The common approach for using PPG to measure blood glucose level (BGL) is to extract features from PPG signals and then apply machine learning models to estimate the BGL. However, most of the existing methods do not meet the clinical requirement, which states that at least 99% of the results must be within zones A and B of the consensus error grid analysis.

In this study, we propose a novel machine learning algorithm for non-invasive blood glucose measurement using PPG signals. We use the largest public dataset (MIMICIII) to train and test our algorithm. We also develop a signal processing and feature extraction pipeline to improve the accuracy of the BGL estimation. Our results show that our algorithm achieves 93.6% accuracy, with 96.15% of the data in zone A and 3.85% of the data in zone B. This is an improvement over the state-of-the-art methods. We are currently working on optimizing our algorithm and designing a specific device for glucose measurement. We believe that our method has the potential to reach the clinical accuracy and benefit millions of diabetes patients.

2 Objectives

To evaluate the blood glucose level detection capability of the PPG approach, a study is required to compare the PPG method and the traditional invasive blood glucose testing method. Since this study mainly focuses on the blood glucose level of healthy people as a proof of concept, only healthy subjects will be recruited.

3 Data Delivery

1. The answers of personal attributes
2. The heart rate in bpm
   (a) at time 0 min (blood glucose baseline)
   (b) at time 30 mins
3. The 8-minute PPG signal
   (a) at time 0 min (blood glucose baseline)
   (b) at time 30 mins

4. Blood glucose level
    (a) at time 0 min (blood glucose baseline)
    (b) at time 30 mins

4 Study Protocol

This study will be conducted according to the Declaration of Helsinki's ethical principles for medical research on human subjects. Informed consent will be obtained from each participating subject. This protocol refers to the Endocrinology Handbook published by Imperial College Healthcare NHS Trust [3].

4.1 Selection of the subjects

4.1.1 Source of subjects

COCHE, Hong Kong

4.1.2 Target number of subjects

50

4.1.3 Inclusion Criteria

- Healthy people between 18 and 65 years old

4.1.4 Exclusion Criteria

- Patients with implantable cardiac devices, including permanent pacemakers, cardiac-resynchronization therapy or defibrillator
- Pregnant people
- People who are unable to sign the informed consent

5 Study Workflow

5.1 Personal attributes

1. Age
2. Gender
3. Height (cm)
4. Weight (kg)
5. Time elapsed from the last meal (hours)
6. Ethnicity
    - White (white)
    - East Asian (east_asian)
    - West Asian (west_asian)
    - Middle Asian (middle_asian)
    - South Asian (south_asian)
    - Southeast Asian (southeast_asian)
    - African Americans (african_americans)
    - Hispanic and Latino Americans (hispanic_and_latino_americans)

- Caribbean or Black (caribbean_or_black)
- Other (other)

7. Diabetes situation
   - No diabetes (no)
   - Type 1 diabetes (type_1)
   - Type 2 diabetes (type_2)
8. The total number of cigarettes consumed from this time last year to the present moment
   - 0 (a)
   - 1-50 (b)
   - >50 (c)
9. The monthly average number of times alcohol was consumed from this time last year to the present moment
   - 0 (a)
   - 1-2 (b)
   - >2 (c)

5.2 Preparation of the Subject

- Fast overnight such that there is no food intake for at least **six** hours.

5.3 Preparation of the Researcher

5.3.1 On the Day before the Experiment

1. Prepare oral glucose load
   (a) Buy bottles of original-taste Lucozade (70 kCal/100mL formulation)

5.3.2 On the Day of the Experiment

1. Prepare a quiet and relaxing environment without ambient noise.
2. Use a measuring cup to prepare 440 mL of Lucozade drink in room temperature.
3. Prepare the Contour plus ELITE blood glucose monitor
   - Test paper.
   - Replaceable needles.
4. Prepare the alcohol wiper for sterilization.
5. Prepare the Finapres device.
   (a) Connect the SpO2 sensor to the Finapres device.
   (b) Switch on the Finapres device.
   (c) Press 'Setup and start measurement'.
   (d) Press 'Continue'.
   (e) Press 'Reload patient data'.
   (f) Press 'Continue'.
6. Prepare the Analog Devices PPG device.
   (a) Connect the ADPD4200 motherboard to the computer.
   (b) Switch on the motherboard. Two LED lights should be ON.

(c) Connect the AFE board to the motherboard.

(d) Open the Wavetool Evaluation software.

(e) Load the configuration.

(f) Open C, D and E slots.

7. Prepare a stopwatch.
8. Prepare a timer and set the time to 8 minutes.
9. Prepare tissues.
10. Open the excel file from the folder 'ideation_lester/ogtt' for recording the personal attributes, the blood glucose level and the PPG file name.

5.4 Procedures

1. Invite a subject who has fasted overnight.
2. Ask the subject to sign the consent form.
3. Ask the subject to fill in the diabetes questionnaire.
4. Ask the subject for his/her personal attributes and record the answers
5. Ask the subject to sit comfortably on a chair in the prepared environment.
6. Ask the subject to place the left arm onto the table in a comfortable position.
7. Read the blood glucose level with the blood glucose monitor.

   (a) Sterilize the whole blood glucose monitor setup with alcohol.

   (b) Place a new replaceable needle into the cartridge of the finger puncturing tool.

   (c) Sterilize the right-hand index fingertip with alcohol.

   (d) Insert the test paper into the blood glucose monitor.

   (e) Ask the subject to use the finger puncturing tool to puncture the right-hand index fingertip.

   (f) Ask the subject to absorb the blood with the blood glucose test paper.

   (g) Collect the used puncturing tool as a medical waste.

   (h) Provide the subject with tissues to cover the wound on the fingertip.

   (i) Read and record the blood glucose level to the excel file.

8. Use the Finapres device to get the heart rate in bpm.

   (a) Clip the SpO2 sensor onto the subject's left index finger.

   (b) When there is a stable heart rate, record it to the excel file.

   (c) Remove the SpO2 sensor from the subject's left index finger.

9. Use the Analog Devices device to get the PPG signal.

   (a) Fix the PPG sensor onto the subject's thumb with the Finapres clip and a black velcro tape.

   (b) Start logging the PPG signals.

   (c) Start the timer.

   (d) Stop recording the PPG signals when the time is up.

   (e) Save the PPG signals and record the file name in the excel file.

   (f) Remove the PPG sensor from the subject's left hand.

   (g) Move the logged data folder to 'ideation_lester/ogtt/ppg'.

10. If the blood glucose level is higher than 6.9 mmol/L, test the level again [1].
11. If the level is still higher than 6.9 mmol/L, stop the experiment at this point. Suggest the subject that he/she should seek professional medical consultation.
12. Ask the subject to drink the 440 mL of Lucozade drink within 5 minutes.
13. Start the stopwatch (time = 0 min).
14. Repeat steps 6-9 when the stopwatch shows 30 mins.

References

[1] Indicator Metadata Registry Details. https://www.who.int/data/gho/indicator-metadata-registry/imr-details/2380.

[2] Blood Glucose Meter Market Size, Share and Industry Analysis by Product (Continuous Glucose Monitoring Devices, Self-Monitoring Blood Glucose (SMBG) Systems), By Technique (Invasive, Non-Invasive), By Type (Wearable, Non-Wearable), By Distribution Channel. Technical report, Fortune Business Insights, July 2019.

[3] Sarah Ali, Channa Jayasena, and Matthew Allum. *Endocrinology Handbook*. Imperial College Healthcare NHS Trust, 2018.

[4] Enikö Vargová and Andrea Němcová. Estimation of blood glucose level based on PPG signals measured by smart devices. In *Proceedings II of the 29st Conference STUDENT EEICT 2023: Selected papers.*, pages 137–140, Brno, Czech republic, 2023. Brno University of Technology, Faculty of Electrical Engineering and Communication.