Study Report

SPECTROPHON Glucometry Monitor Accuracy Study

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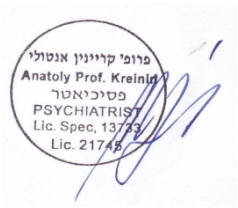
Principal Investigator: Prof. Anatoly Kreinin, MD, PhD



Co-Principal Investigator: Prof. Albert Pinhasov, PhD

Project Leader: Dmitry Rodin, PhD

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1. Study information and Objective

Diabetes is a chronic, life-long disease that represents a major public health challenge globally (Matthews et al 1985) More than 346 million people worldwide have diabetes mellitus, and it is predicted to become the seventh leading cause of death by the year 2030 (Golden et al. 2012). To maintain blood glucose level homeostasis, repeated blood glucose testing is needed. The vast majority of currently available methods for blood glucose testing are invasive and cause discomfort for patients. However, biosensors have recently become a promising solution for non-invasive glucose blood testing (Bandodkar et al 2014; Zhang et al 2015). Spectrophon LTD has developed a technology that allows measurement of even the smallest amounts of various compounds contained in sweat. Using a unique algorithm developed by Spectrophon LTD, this methodology provides the possibility of evaluating levels of chemicals in the bloodstream. Based on this technology, Spectrophone LTD has developed a glucometer monitor (NIGM) that is able to non-invasively detect the blood glucose level. This glucometer biosensor can be easily incorporated into most commercially available smartwatches. Development of this technology will allow real-time, non-invasive measurement of blood glucose level and will dramatically facilitate effective treatment of diabetes.

The main **objective** of current study is to estimate the accuracy of NIGM incorporated in smartwatches Samsung Gear S2. The secondary **aim** of the study is to evaluate the safety-in-use of NIGM.

Study variables and end points:

Blood glucose level – 2 times per experiment

Visual examination of the skin contacting the sensor - at the end of the experiment

2. Test Facility

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3. Tested device

Name: Glucometry Monitor
Source: Spectrophon, LTD
Model: SP-NIGM
Firmware version: 1.7

4. Experimental Design

This study examined the accuracy of Spectrophon NIGM incorporated in smart watch Samsung Gear S2 that non-invasively and indirectly detects the level of glucose in human blood. Metabolic syndrome and type 2 diabetes mellitus appears to be more prevalent in the psychiatric setting than in the general population, so Maale Carmel Mental Health Center (MCMHC) was chosen for conducting the trial (Roberts et al. 2017). Adult participants (n=200) were recruited for the study from the staff of MCMHC (including doctors, nurses and administrative workers; no psychiatric in-patients were recruited for the study). Participants were mainly Israelis with skin color to fit Fitzpatrick type IV (dark intermediate). In parallel to glucose measurements with NIGM, blood was collected from the cubital vein for an additional measure of blood glucose.

The participants were able to select between two options for blood collection:

First option: Intravenous cannula (Venflon) was inserted in the cubital vein and blood collected twice in the beginning and end of the procedure (within one hour), then assessed for the glucose level with YSI 2300 STAT Plus Glucose Analyzer (YSI 2300).

Second option: The blood was collected twice from the cubital vein at the beginning and end of the procedure (within one hour) and checked for the glucose level with YSI 2300.

The measurements were performed twice: before food intake and after food intake, with 1-3 hour interval between measurements.

The results of the measurements obtained from NIGM were compared to the results obtained from the YSI 2300.

Evaluation of the accuracy of NIGM was defined as the difference between subject blood glucose level measured by YSI 2300 and blood glucose level non-invasively measured by NIGM.

All experiments were conducted indoors under ambient temperature (22-24^{o}C) and humidity (40-60%).

4.1. Experimental groups:

Number of subjects: 200 (both genders)

Age range: 18-75

4.2. Inclusion criteria:

Healthy individuals between ages 18 and 75 that were able to sign informed consent form.

4.3. Exclusion criteria:

Acute psychotic state, hepatitis or HIV, tuberculosis, diabetes, hemophilia and other serious coagulation disorders, significant impaired venous access, pregnancy.

5. Procedures:

Blood glucose level was examined twice:

I. First measurement

NIGM was applied to the participant's skin after taking a blood sample from the cubital vein. NIGM non-invasively measured glucose level in triplicate samplings.

After blood sampling, the participant received food.

II. Second measurement

Between measurements, participants were allowed to continue their usual activities without any restriction. After first measurement (1-2 hours) and not earlier than 30 minutes after food intake, the second blood sample was collected from the cubital vein. After taking blood sample, NIGM was applied again to participant's skin and non-invasively measured glucose level in triplicate samplings.

5.1. Data recording:

Results obtained from NIGM were automatically archived on a mobile phone Bluetooth-linked to a Samsung Gear S2. Manual recording of data was also conducted.

5.2. Food intake:

There were no limitations to food type and quantity. Participants were recommended to consume drinks and food with sugar.

5.3. Restrictions:

See exclusion criteria.

Participants could cancel the experiment at any point of the procedure if desired.

6. Results

All participants finished the planned procedure with no incidents to report.

Subject skin was examined after the procedure to ensure that no allergic reaction or any other reaction related to hypersensitivity were caused by NIGM. No adverse skin reactions were observed.

In some cases, the level of blood glucose reduced after food intake that can be possibly explained by reactive hypoglycemia occurring occasionally both in diabetic patients and healthy individuals.

For glucose measurements obtained **before** food intake, the overall difference between glucose level measured using commercially available glucose analyzer YSI 2300 and glucose level measured by Spectrophon NIGM did not exceed 15 mg/dL (for measurements in range 0-100 mg/dL) or 15% (for measurements greater or equal to 100 mg/dL) in 95% of all samples (190 measurements out of total 200 samples - see Fig. 1 for distribution of measurement errors and differences).

For glucose measurements obtained **after** food intake the overall difference between glucose level measured using commercially available glucose analyzer YSI 2300 and glucose level measured by Spectrophon NIGM did not exceed 15 mg/dL (for measurements in range 0-100 mg/dL) or 15% (for measurements greater or equal to 100 mg/dL) in 95,5% of all samples (191 measurements out of total 200 samples - see Fig. 2 for distribution of measurement errors and differences).

7. Summary

Out of 200 measurements conducted by Spectrophon NIGM, less than 5% differed from the blood glucose level measured by the invasive method with YSI 2300 more than 15% (or 15mg/dL).

Obtained results allows us to conclude that NIGM developed by Spectrophon LTD is an accurate tool for glucose level measurement.

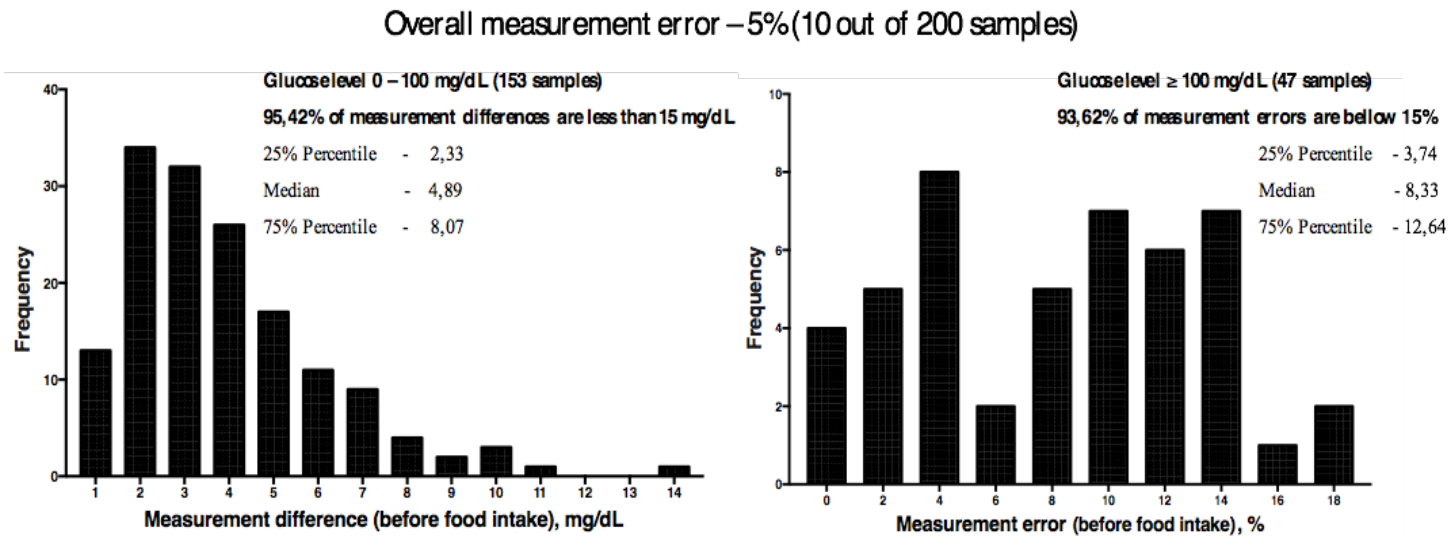

Fig.1 Frequency of measurement error (before food intake)

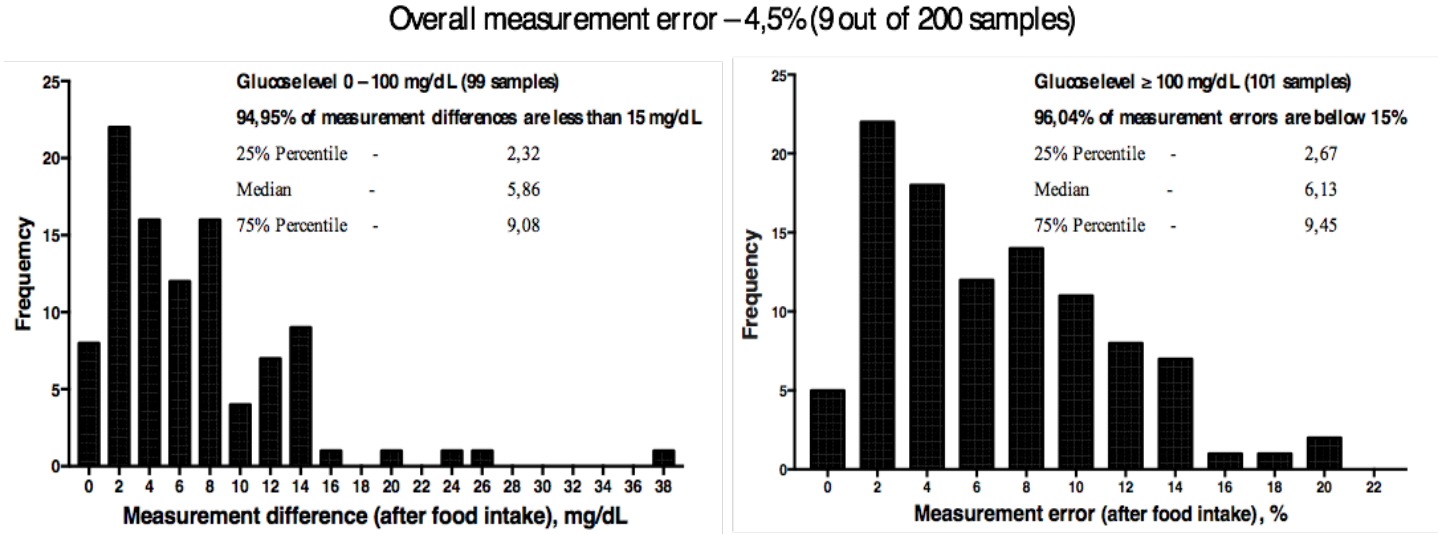

Fig.2 Frequency of measurement errors (after food intake)

7. Appendix 1. Results on additional glucose level tests for participants with glucose level higher than 200 mg/dL

For glucose measurements of blood obtained from participants with glucose level higher than 200 mg/dL, the overall difference between glucose level measured using commercially available glucose analyzer YSI 2300 and glucose level measured by Spectrophon NIGM did not exceed 15% in 100% of all samples (34 measurements out of total 34 samples - see Fig. 3 for distribution of measurement errors).

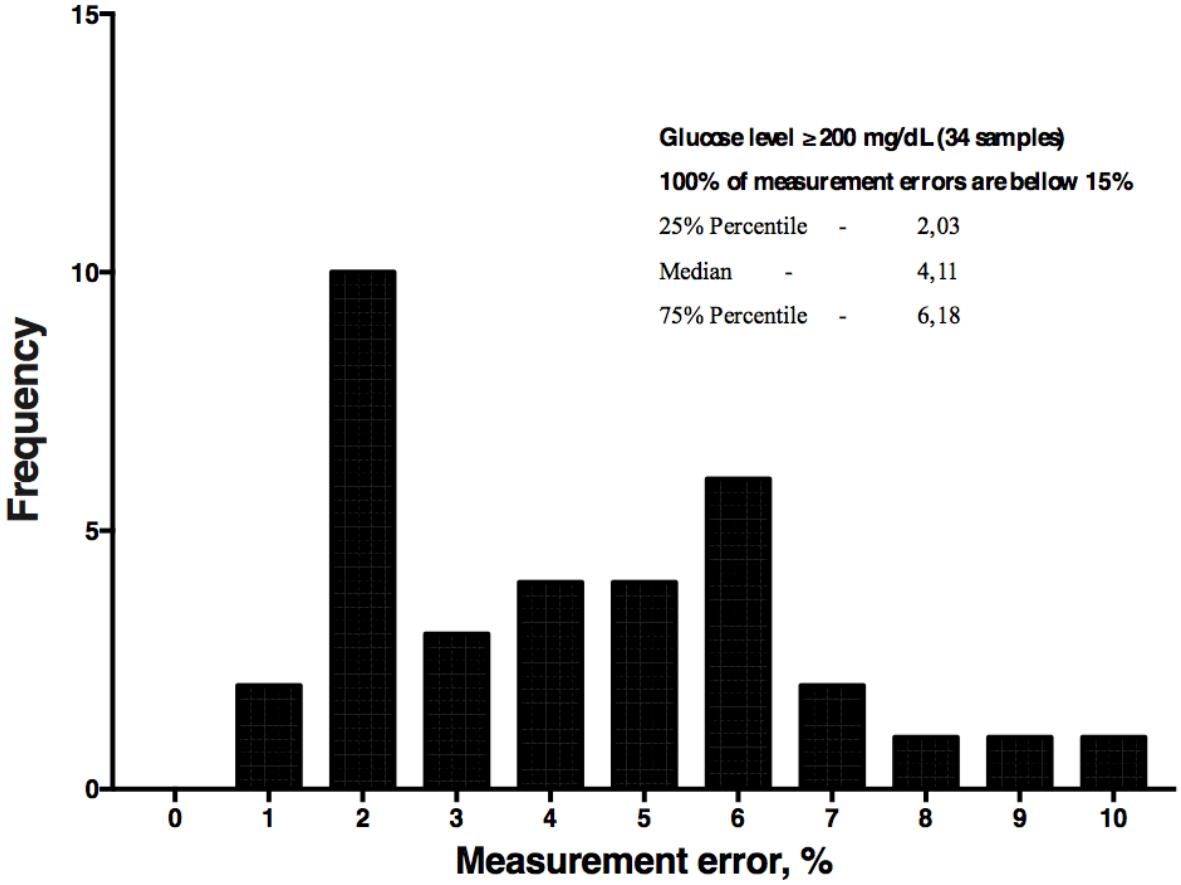

Fig.3 Frequency of measurement errors (for glucose level ≥200 mg/dL)

8 References

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