Non-invasive Measurement of Blood Glucose, Blood Pressure and Extrapolation of QRS Complex Using a Wrist Wearable Photoplethysmography Sensor

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IRB Minimal Risk Protocol Template

Note: If this study establishes a human specimen repository (biobank) for research purposes, do not use this template. Use the Mayo Clinic Human Specimen Repository Protocol Template found on the IRB home page under Forms and Procedures at [redacted]

First-time Use: Use this template to describe your study for a new IRB submission.

1. Complete the questions that apply to your study.
2. Save an electronic copy of this protocol for future revisions.
3. When completing your IRBe application, you will be asked to upload this document to the protocol section.

Modification: To modify this document after your study has been approved:

1. Open your study in IRBe. Click on the study 'Documents' tab and select the most recent version of the protocol. Save it to your files.
2. Open the saved document and activate "Track Changes".
3. Revise the protocol template to reflect the modification points , save the template to your files
4. Create an IRBe Modification for the study and upload the revised protocol template.

General Study Information

Principal Investigator: Narayan (Guru) Kowlgi, MBBS, FACC, FHRS

Study Title: Non-invasive measurement of blood glucose, blood pressure and extrapolation of QRS complex using a wrist wearable photoplethysmography sensor

Protocol version number and date: V1, November 10, 2022

Research Question and Aims

Hypothesis: A non-invasive wrist-based photoplethysmography (PPG) sensor may detect changes in blood glucose level and blood pressure. The PPG signal may also be used to extrapolate a waveform that may be used as a surrogate for the cardiac QRS complex.

Aims, purpose, or objectives:

1. Measure systolic and diastolic blood pressure detected by a wrist-based sensor and compare against standard of care noninvasive cuff blood pressure measurements and/or invasive arterial line measurements.
2. Extrapolate a surrogate waveform for the cardiac QRS complex by training and validating against the reference electrocardiograph (ECG) waveform.
3. Measure blood glucose levels detected by a wrist-based sensor and compare against fingerstick data obtained four times daily in hospitalized diabetic patients
4. Measure blood glucose levels detected by a wrist-based sensor and compare against whole blood glucose identified in hospitalized patients undergoing anticipated blood glucose measurements

Background (*Include relevant experience, gaps in current knowledge, preliminary data, etc.*): Diabetics on insulin or several oral agents need to monitor blood sugar several times daily. However, checking blood sugar is invasive, requiring at minimum finger stick monitoring, and thus may be prone to issues with compliance. Recent data has suggested that spectral signatures that may be obtained using specific light frequencies over superficial vessels may allow for noninvasive measurement of blood glucose levels, including changes in levels over time. This may allow for non-invasive measurement of blood glucose that may permit pre-diabetic and diabetics to improve continuous and intermittent approaches to monitoring.

Additionally, we are at a paradigm shift in medicine where we are moving away from the traditional 6-monthly or annual follow-ups and entering an era of continuous monitoring. The novel wrist-based photoplethysmography (PPG) sensor would be able to measure systolic and diastolic blood pressure noninvasively and without the sensation of manual pressure. Thus, we can acquire many more data points on patients and potentially detect disease exacerbations before it is too late.

Study Design and Methods

Methods: *Describe in lay terms, completely detailing the research activities that will be conducted by Mayo Clinic staff under this protocol.*

Patients will be asked to wear a wrist-based PPG sensor (LifePlus, Inc) that will be worn throughout their hospitalization. They will be identified on the basis of being diabetic with anticipated four times daily blood glucose checks to be done as part of their regular inpatient care. Data collected will include patient demographics, body mass index, and Fitzpatrick skin tones. Timing of fingerstick checks as well as labs in which whole blood glucose measurements are obtained will be recorded and synchronized against evaluations recorded by the wrist-based sensor. These will then be compared offline for accuracy. Similar comparisons will be made for blood pressure readings and compared to standard vital sign checks on the floor.

For blood pressure measurements, we will additionally study patients who undergo electrophysiologic procedures. We will compare readings on the wrist-based sensor to invasive arterial line measurements and/or noninvasive blood pressure readings obtained via a cuff-inflation in studies such as the tilt-table test. We typically monitor the electrocardiograph (ECG) waveform on these patients as well. During this study, we will collect continuous, time-synced PPG, blood pressure and ECG data from these patients for the duration of the procedure.

Subject Information

Target accrual is the proposed total number of subjects to be included in this study at Mayo Clinic. A "Subject" may include medical records, images, or specimens generated at Mayo Clinic and/or received from external sources.

Target accrual: 200 patients (100 patients hospitalized, and 100 patients undergoing EP procedures)

Subject population (children, adults, groups): adults

Inclusion Criteria:

1. Diabetic patients on insulin undergoing four times daily blood sugar checks as part of standard of care.
2. Patients undergoing continuous monitoring for heart rate, ECG and blood pressure as part of their routine care.
3. Patients undergoing invasive and noninvasive electrophysiologic procedures.

Exclusion Criteria:

1. Patients unable to provide informed consent
2. Patients without arms as these are needed to wear the wrist-based sensor

Data Analysis

Power analyses may not be appropriate if this is a feasibility or pilot study, but end-point analysis plans are always appropriate even if only exploratory. Provide all information requested below or provide justification if not including all of the information.

Power Statement: This is a pilot study and thus is not specifically powered to reach a hard outcome. After this exploratory analysis, we will use this to appropriately power a larger study.

Data Analysis Plan: The data will be acquired with direct synchronization between glucose levels obtained by fingerstick or whole blood measurements and blood pressure (manually and invasive arterial line), ECG waveform and from the wrist-based PPG sensor. We will then compare the change in glucose level and blood pressure between measurements estimated by the sensor and by the standard glucose measurements. We will compare the changes in parameters between measurement time points using the standard measurements versus the wrist-based sensor using standard statistical methods (paired student t-test or Wilcoxon Signed Rank test). We will also evaluate what the absolute differences are between the 2 measurement approaches to determine the clinical significance. For the ECG comparison study, we plan to extrapolate a surrogate waveform from PPG and validate it against the reference QRS complex from the ECG waveform.

Endpoints
Primary:

1) Difference between measurement of systolic and diastolic blood pressure using the wrist-based PPG sensor versus standard cuff-inflation and invasive measurement of blood pressure.
2) Difference between a surrogate waveform extrapolated from wrist-based PPG sensor versus standard QRS complex reported by the ECG sensor.
3) Difference between measurement of blood glucose level using the wrist-based PPG sensor versus standard blood-based measurement of blood glucose.

Secondary: N/A