The DEPART Device: A Continuous Ambulatory Blood Pressure Monitor

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Abstract

Hypertension affects an estimated 45% of Americans and is considered one of America's major health problems.[1] Continuous ambulatory blood pressure monitors (cABPMs) have the potential to benefit affected individuals by providing accurate, long-term readings into their blood pressure patterns. For this purpose, Barron Associates designed the DEPART System, an ergonomic, cost-effective cABPM that collects PPG and ECG data to make blood pressure measurements. We aimed to build on past work with the device by (1) collecting data using the DEPART System and a criterion device, the Human NIBP Nano System, and (2) using MATLAB to process the data and model blood pressure under different conditions. Regression models were created for diastolic and systolic blood pressure for two subjects' data sets, where heart rate and either pulse arrival time (PAT) or differential pulse arrival time (dPAT) served as independent variables. PAT, calculated for chest and finger PPG sensors, was found by subtracting the peak points of each PPG waveform from the peak points of the corresponding ECG waveform. dPAT was found by subtracting the finger and chest PAT readings. The regression models were then evaluated relative to standards set by the Association for the Advancement of Medical Instrumentation (AAMI), which they did not meet. Further research with the DEPART system should involve more subjects, more inputs (such as heart rate variability metrics), different criterion systems (such as the Caretaker), and explorations of machine learning and deep learning algorithms to make blood pressure predictions.

Keywords: Hypertension, Continuous Ambulatory Blood Pressure, Pulse Arrival Time, Differential Pulse Arrival Time

Introduction

Background

Hypertension describes the condition of having excessively high blood pressure for prolonged periods. It can cause progressive damage to the body over time, negatively impact quality of life, and drastically increase someone's risk of having a heart attack or stroke. The CDC defines hypertension as blood pressure exceeding 130/80 mmHg, and in 2018, it was cited as a primary or contributing cause to nearly 500,000 deaths.[1] It has been estimated that, in the United States, 45% of adults have hypertension, but only about 24% of those people have their condition "under control".[1] Additionally, hypertension treatments comprise a significant portion of health care expenditures; in 2006, such expenditures were estimated to be nearly $55 billion.[2] Between 1999 and 2016, the overall burden of hypertension in the United States has increased, indicating the need to enhance prevention and treatment efforts.[3]

In the past, any system that claimed to be a beat-to-beat blood pressure monitoring method required an invasive procedure involving arterial catheters or other complex devices. Given the complex nature of these procedures, these methods were reserved for critical care settings.[4] This left a need for a more current, non-invasive model not limited to critical care. ADInstruments' solution is the Human Non-invasive Blood Pressure (NIBP) Nano system, which allows for the measurement of a continuous blood pressure signal using a dual finger cuff system.[5] This device can correct for motion artifacts using a Height Correction Unit (HCU) that accounts for hand movement relative to the heart.[6] The system, however, is not convenient to use in day-to-day life, as it consists of a wrist unit, finger cuff, and a 3 meter long cable connecting the wrist unit to an interface that facilitates communication with a data analysis software called LabChart.

Recent studies show that the most accurate blood pressure measurements are both ambulatory and self-monitoring. Ambulatory monitoring has become the gold standard for predicting clinical risk related to blood pressure, as it has been found to be a better predictor than conventional blood pressure monitors. Additionally, self-monitoring device eliminates blood pressure increases that often occur in doctor's office and allows for multiple readings to take place over a prolonged period of time.[7,8] Currently there is not an effective 24-hour, self-monitoring, ambulatory system that is widely available to diagnose hypertension. Additionally, the devices on the market are too expensive to allow patients to monitor their responses to treatments and understand their effectiveness. For these reasons, Barron Associates has developed a continuous blood pressure monitor with the potential for self-monitoring and ambulatory use. The system aims to monitor blood pressure on a heartbeat-to-heartbeat basis to maximize accuracy and precision while being ergonomic and cheap enough for people to use over long periods throughout the day.

The system utilizes differential pulse arrival time (dPAT), determined from the pulse arrival time (PAT) measured at each patch. PAT is the length of time it takes for a heartbeat to travel from an ECG signal at the chest to a PPG signal at a different point in the body. PAT has been studied in depth, and has been determined to be proportional to blood pressure in a number of different regression and machine learning models.[9–13] However, in other studies, PAT has been found to be inaccurate because of the inclusion of a pre-ejaculation period (PEP).[14–16] In previous studies, dPAT has also been previously been found to be a valid and accurate measure of blood pressure, as well, as it removes the PEP.[17]

The dPAT does not account for specific physiological factors that may influence the blood pressure reading, for example changes in sympathetic tone.[13] The DEPART algorithm will account for sympathetic nervous system effects on the arterioles through the inclusion of heart rate variability, which has been shown to correlate with autonomic tone.[18] The sympathetic nervous system can modulate blood vessel diameter through nervous system innervation of the vascular smooth muscle in response to real-life stressors, including college examinations.[19] This measure has been extracted from smartphone photoplethysmograms (PPG), and will be found using PPG technology in the DEPART device.[20] The use of machine learning to help determine patterns within the blood pressure data is another aspect of the device.[21] Our contribution to this device will be determining if dPAT is a more effective metric for finding blood pressure than PAT, and determining if HRV improves the blood pressure model.

This device will contribute to public health by improving the diagnosis of hypertension, allowing for better correlations between hypertension diagnosis and clinical outcomes. It will do this by allowing for 24-hour continuous monitoring for patients with blood pressure irregularities and providing comprehensive data about their cardiovascular patterns. This should enable clinicians to recognize hypertension sooner in patients' lives and do so more reliably. For patients, the device will be cheaper and more accessible than the current standard for continuous monitoring, as well as easier to use and less invasive. Its decreased sensitivity to motion artifacts will allow for more mobility, and its placement and relatively small size should minimize interference with daily activities. By better informing clinicians and providing more comfort for patients, the system could decrease rates of hypertension and associated morbidities, including heart failure, stroke, and dementia. In addition to benefiting public health, the more comprehensive data about blood pressure patterns could bolster scientific knowledge regarding how the body works and how hypertension correlates with diseases.

Aims

The first aim involves collecting human subjects' blood pressure data to test the efficacy of Barron Associates' continuous (beat-to-beat) ambulatory blood pressure monitor, known as the DEPART system, relative to the Human NIBP Nano, a currently used FDA-approved system. This testing will allow the team to collect human subjects' data through an IRB-approved study utilizing both devices for comparison.

The second aim is to use data obtained through testing to create regression models using either dPAT or PAT. For the regression inputs, PATs from the chest ECG signal to the PPG on the chest and to the PPG on the finger were calculated. To find the dPAT, the difference between the finger PAT and the chest PAT was found. This value was believed to eliminate the pre-ejaculation period (PEP) that is present in the PAT, possibly creating a more accurate blood pressure measurement.[14–16] The goal was to determine which estimation method provides a more accurate blood pressure measurement in comparison with the FDA approved Nano System. Additionally, the results from these models were evaluated against the standards set by the Association for the Advancement of Medical Instrumentation (AAMI) to determine their efficacy in the traditional seated posture in which blood pressure is typically measured.

Materials and Methods

Materials

In order to collect human subject's data and fulfill the first specific aim, the team used three main materials in addition to software and laboratory tools for measuring the height and weight of subjects: The Human NIBP Nano monitoring system, the DEPART system, and the Biometrics Hand Grip Dynamometer.

The Human NIBP Nano, which will hereafter be referred to as the "Nano" or "Nano system", consists of two finger cuffs attached to a wrist unit, as well as a three lead ECG on the chest. The entire unit is connected to an interface that provides power to the wrist unit and facilitates communication with a software system that processes and displays data on-screen.[5] The device also features a height correction unit, which allows the system to compensate for movement of the hand relative to the heart.[6] Overall, the Nano system integrates numerous software and hardware components to provide a continuous blood pressure signal from adult humans in a non-invasive manner.

The DEPART system, which is the main experimental focus, consists of a wrist unit and chest unit, these are shown in Figure 1A and 1B, respectively. Each unit utilizes a microSD card that stores the data being recorded, as shown in Figure 1C. The wrist unit attaches to the fingers and wrist, where the wearer can control and manage data collection; it has a PPG sensor embedded in the finger cuff. The chest unit attaches to the sternum via an electrode. For proper data collection, an additional electrode on the left side of the chest connects to an ECG sensor, and an attached PPG sensor is taped elsewhere to the chest. After data is collected from each unit, including ECG and PPG signals from the chest unit and a PPG signal from the wrist unit, the microSD cards from each must be processed with software external to the device to obtain beat-to-beat ECG and PPG data. An example of an output graph of the DEPART

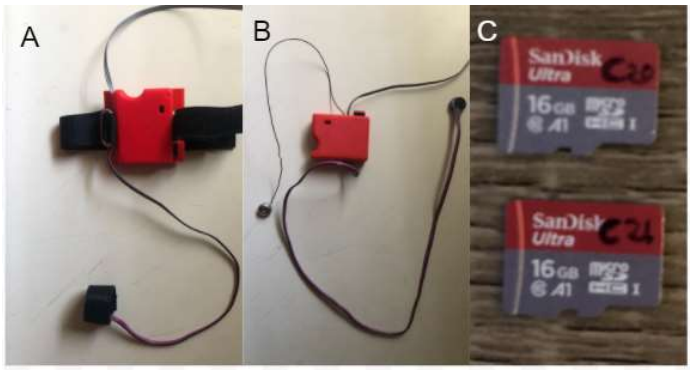

Figure 1: The DEPART Device. The wrist unit of the device, with the finger cuff PPG sensor attached by a wire, is shown in Figure 1A. The chest unit of the device, with both the ECG and PPG sensors connected, is shown in Figure 1B. The microSD cards used in the device are shown in Figure 1C.

data is shown in Figure 2. The Biometrics Hand Grip Dynamometer is used by subjects in the latter portion of the lab protocol to increase sympathetic stimulation and change blood pressure relative to a resting state. By inducing blood pressure changes with the dynamometer, data collection could occur over a broader range of real-world conditions. This allowed for a more comprehensive evaluation of the DEPART system

and the subjects tested. More detail on how the dynamometer was applied is included in the "Lab Protocol" section.

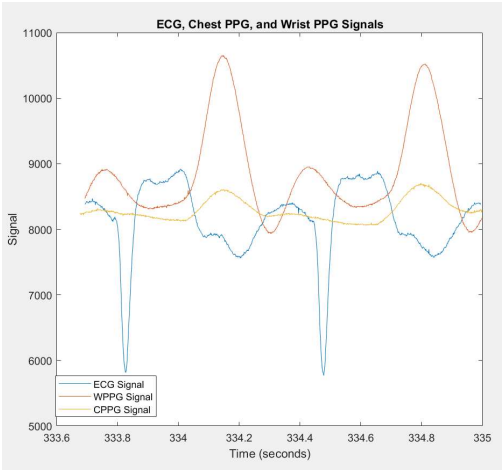

Figure 2: The DEPART Device Raw Data. The signal from the ECG signal is demonstrated in blue, the signal from the finger PPG attached to the wrist unit is shown in red, and the signal from the PPG attached to the chest unit is shown in orange.

Lab Protocol

Subjects were recruited by team members. After subjects' height, weight, and sex, the team simultaneously hooked them up to the DEPART and Nano systems. The Nano was attached to the wrist and index finger of the subject's non-dominant hand, and the DEPART system rPPG sensor was attached to the chest and another DEPART system rPPG sensor was attached to the wrist (or forearm) of the non-dominant hand. The setup of both devices on the subject is illustrated in Figure 3. The subject was asked to jump once to create an artifact within the data in order to

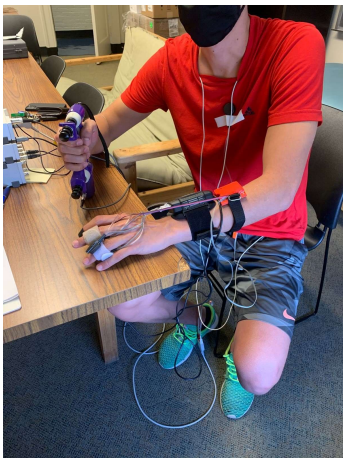

Figure 3: The Laboratory Set-up. The subject is shown attached to both the DEPART device and Nano System. The DEPART system wrist unit is the lower unit attached to the subject's forearm and the black finger cuff. The Nano System is the unit closer to the subject's hand, and it attaches to the two white finger cuffs. In this figure, you cannot see the chest attachments of either device. The subject is also pictured holding the Biometrics Handgrip Dynamometer.

establish a starting point for both sets of data being collected. Each subject's maximum voluntary contraction (MVC) was assessed in the dominant hand before beginning her/his experimental trial using the Biometrics Hand Grip Dynamometer.

ECG and PPG data were recorded simultaneously in the following conditions, in the following order:

1. Seated quietly with their feet flat on the floor and her/his non-dominant upper arm at heart level
2. Lying down
1. Standing still with arms at their sides
2. Standing still with arms raised over head
3. Standing still with straight arms extended 90 degrees
4. Seated while gripping the Biometrics hand grip dynamometer at 10% of MVC
5. Seated while gripping the Biometrics hand grip dynamometer at 20% of MVC
6. Seated while gripping the Biometrics hand grip dynamometer at 30% of MVC
7. Seated while gripping the Biometrics hand grip dynamometer at 40% of MVC

Each condition will be maintained for 3 minutes while recording data with the DEPART and Finapres Nano systems. Subjects will be given a 5-minute rest period between all activities (i.e., arm elevations and hand grip exercises). More rest time will be allowed if needed by the subject following any posture or activity.

ECG Peak-picking

To begin the data analysis the peaks of the ECG were determined. This was needed to determine the RR interval, heart rate variability, and the PATs. The Pan-Tompkins peak picking algorithm was used to find the peak of the R-wave of each ECG. First, a Butterworth filter was applied which is intended to increase the signal-to-noise ratio, then a derivative filter was applied to provide information about the slope of the QRS complex of the ECG signal, and finally, the square of the filter signal was taken to ensure that the R peaks are detected. The graphs of each filter are shown in Figure 4. After the signal has been filtered, the location of each peak is determined and stored in a vector using the peak picking

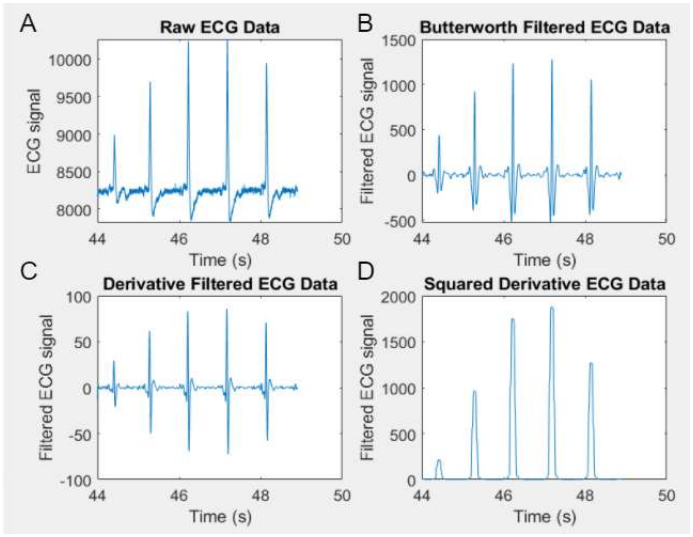

Figure 4: ECG Filtering. The raw ECG data is shown in Figure 1A. A Butterworth filter was applied to the data in Figure 1B. Figure 1C shows the filtered ECG signal after a derivative filter was applied. Figure 1D shows the final squared ECG data.

function on MATLAB. The MATLAB peak picking function requires two inputs, the minimum distance between peaks, and the minimum height of the peaks. The optimal inputs to this function were determined

to be a 0.5 second time delay between peaks, and a peak height of 100. Figure 5 demonstrates the output of this function. To determine the RR interval, each time point was subtracted from the one before it.

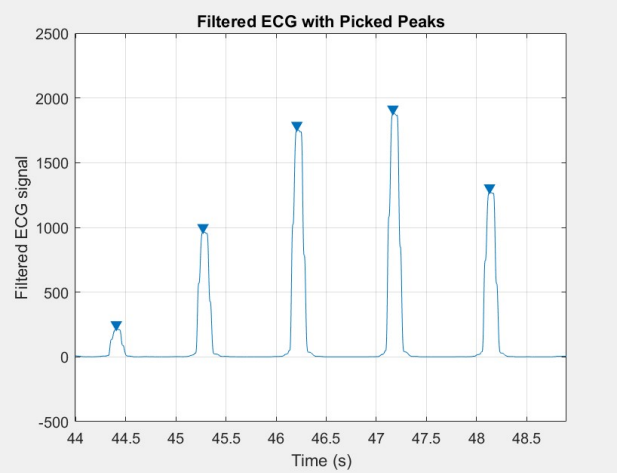

Figure 5: ECG Peak Picking. The blue line illustrates the filtered ECG signal. The blue triangles at the peak of each signal are the triangles chosen by the MATLAB peak picking algorithm. The x and y coordinates of each of these triangles are stored in vectors in MATLAB.

PPG Peak-picking

In order to determine the PAT, a fiducial point must be determined on the PPG waveforms. The team chose to use the peak of the PPG signal as the fiducial point. To find the PPG-peak the same MATLAB peak picking algorithm was introduced. This algorithm was used on both the chest and finger PPG. The inputs used for the chest PPG peak picking algorithm were a minimum height of 300mmHg and a minimum distance of 0.5 seconds. The inputs for the finger PPG were a minimum height of 500mmHg and a minimum distance of 0.5 seconds as well. Figure 6 demonstrates the outputs of this function on a finger PPG waveform.

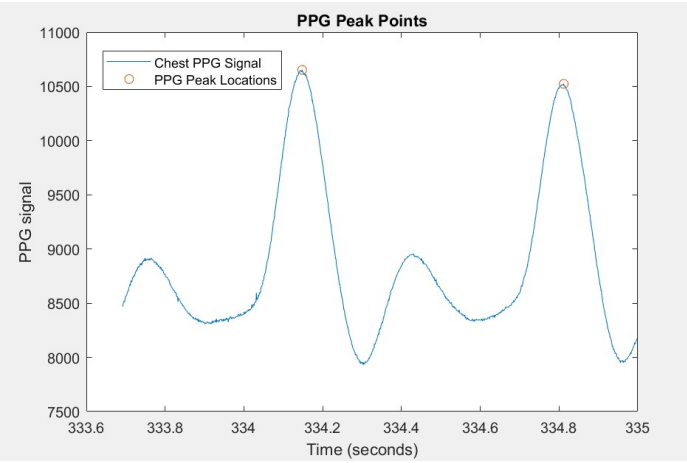

Figure 6: PPG Peak Picking. The PPG peaks were located using the MATLAB Peak Picking algorithm and are shown in this figure as red circles.

PAT and dPAT

The PATs were determined by subtracting the ECG R-peak time point from the PPG peak point. These points are shown in Figure 7. Two PATs were determined, the chest PAT and the finger PAT. Then the dPAT was determined by subtracting the wrist PAT from the finger PAT. These values were then used as inputs into four different regression analysis models.

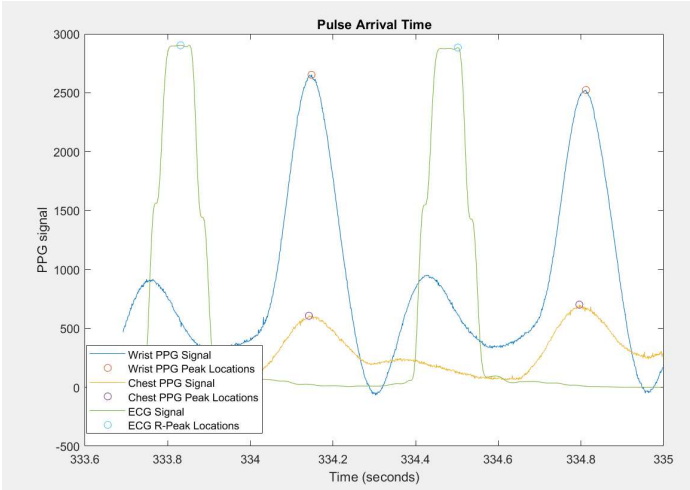

Figure 7: Peak Points of all Waveforms. This figure demonstrates the peak points found from each of the waveforms. The difference between the PPG peaks and each of the ECG peaks were then found to determine the PAT.

Heart Rate Variability Metrics

Heart rate variability (HRV) quantifies short term fluctuations in heart rate, which depend on the activity of the parasympathetic and sympathetic branches of the nervous system; too little or too much HRV can indicate disease or non-ideal health. Because HRV was expected to change between the conditions tested in the in-lab protocol, we aimed to account for it and use a metric for it as an input for the regression model. Using peaks found with the ECG peak picking code, HRV was quantified in two different ways: spectral analysis of low frequency and high

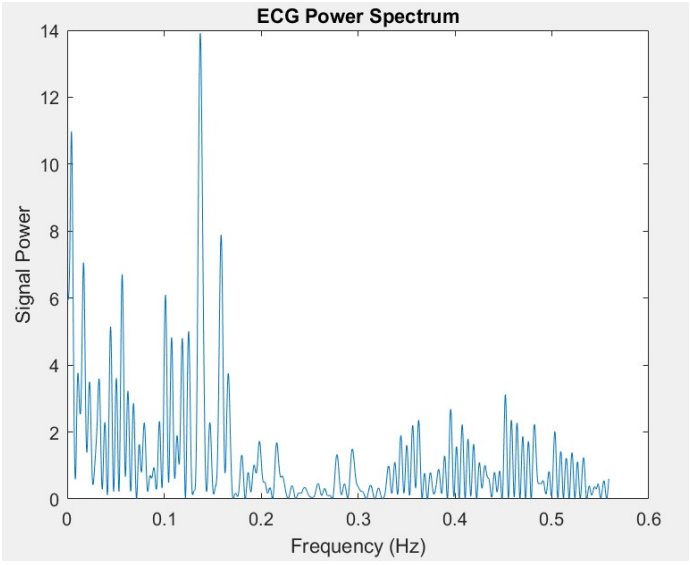

Figure 8: ECG Power Spectrum. The ECG Power Spectrum shows the amplitudes of different frequencies contained in an ECG waveform. The low frequency (0.04 - 0.15 Hz) and high frequency (0.15 - 0.4 Hz) components can be divided and used as a metric for heart rate variability.

frequency components of the ECG as shown in Figure 8 and calculating the root mean square of successive differences (RMSSD) between heartbeats.[22] However, the spectral analysis yielded too few data points to successfully run the regression with, and the RMSSD calculations (N=3) was not found to significantly affect the team's goal of comparing blood pressure models using the chest PAT, finger PAT, or dPAT. Therefore, no HRV metrics were included as inputs in the final blood pressure models, even though they could provide more accurate comparisons between conditions of lower stress (e.g., sitting) and higher stress (e.g., squeezing a hand grip dynamometer). Unfortunately, this metric was determined to be insignificant when used as an input to the stepwise regression model, which we will discuss in the results section.

Results

To assess whether or not PAT or dPAT yielded a better model when predicting blood pressure measurements for the DEPART system, we used regression analysis. In particular, linear stepwise regression was chosen as the model with a 10-fold validation due to its ability to determine which variables are significant to the final model.[23] Every model was developed in MATLAB using the regression learner application and evaluated in Excel.

The PAT data for subject two was not aligned correctly in testing so we decided to train and evaluate each model on only subject one's data. We divided the data in half to create two testing sets. The independent variables that were chosen reflected this significance in the final model. The variables that were significant to the model were heart rate and either PAT or dPAT. We also included the inverses of the PAT or dPAT and the HRV, but they were determined to be insignificant to each model. The output for each model was either systolic or diastolic blood pressure. Each model is shown in figures 9-10. The root mean square error (RMSE) and R^2 values are shown in table 1 below. The models were fairly similar to each other but did not accurately predict the "true" blood pressure values. Equation 1 and Equation 2 show the base equations used to fit the models for PAT and dPAT respectively, with the lower-case variables being coefficients spit out by the model.

$$DBP\ or\ SBP = Intercept + a * FingerPAT + b * ChestPAT + c * HR + d * (Combinations) \quad [1]$$

DBP and SBP refer to diastolic and systolic blood pressure, respectively. HR is the heart rate and (Combinations) are the various combinations that can be justified by the model of the independent variables.

$$DBP\ or\ SBP = Intercept + a * dPAT + b * HR + c * HR * \text{dPAT} \quad [2]$$

Similar to Equation 1, DBP and SBP refer to diastolic and systolic blood pressure, respectively, and HR is the heart rate.

Typically, a lower RMSE is preferred when creating predictive models. Conversely a higher R^2 value is preferred, with the R^2 value representing the correlation coefficient of the fitted model to the data.[24] The R^2 value being below 0.5 is not a good indicator of the fits of the models.[13] This is why both the PAT and dPAT models are similar to each other but not the true blood pressure reading measured with the Nano system. Overall, the PAT model had both higher R^2 values and lower RMSE values, so we chose the PAT models as our final model. It is important to note, again, that the two models are similar to each other but neither are good fits.

Statistical Analysis

Each model in Figures 9-10, has an associated RMSE and R^2 value shown in Table 1 below. When a paired two-sample t-test was performed on the RMSE values with a p-value of 0.05, the difference between the errors was not significant.

In order for a blood pressure monitor to be considered accurate it must meet the standards set out by the AAMI. These standards are for a position that is seated quietly, with the feet on the floor, and the cuff at heart height.[25] In order to meet these standards, the mean difference between each individual systolic and diastolic reading when compared to the test system (in this case the Nano System) must be within ±5mmHg, and the standard deviation of these values must be within 8mmHg.[25] As shown in table 2, these standards were not met by any of the models. This outcome was expected due to the low number of subjects and data points in the model. In Phase I clinical testing, done by Barron Associates, the DEPART system was successfully validated for accuracy and precision relative to a criterion system so our data was the likely error.[26]

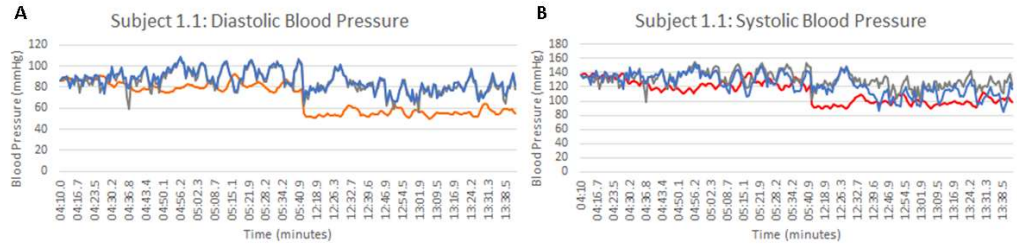

Figure 9: Subject 1.1 Blood Pressure. The diastolic blood pressure (A) and systolic blood pressure (B) are shown in the two graphs above for subject 1.1. The gray line represents the PAT model and the blue line represents the dPAT model on both graphs. The graphs only show the first two conditions (the sitting and lying down conditions) in order to make the graphs readable.

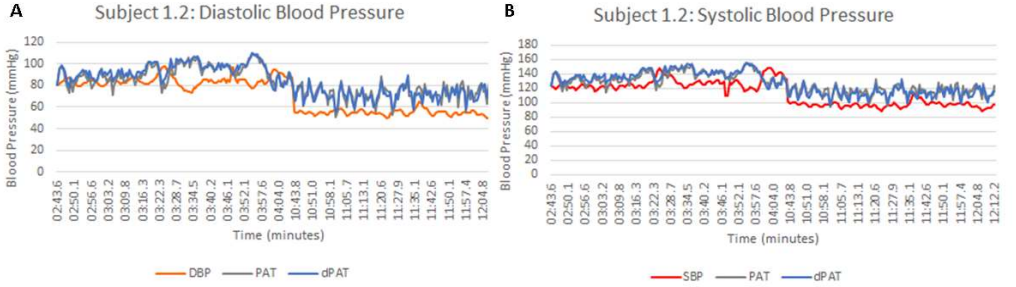

Figure 10: Subject 1.2 Blood Pressure The diastolic blood pressure (A) and systolic blood pressure (B) are shown in the two graphs above for subject 1.2. The gray line represents the PAT model and the blue line represents the dPAT model on both graphs. The graphs only show the first two conditions (the sitting and lying down conditions) in order to make the graphs readable.

Table 1: Regression Model Statistics

			RMSE	R^2
PAT	S1.1	DBP	14.74	0.46
		SBP	16.82	0.46
	S1.2	DBP	13.63	0.54
		SBP	16.37	0.50
dPAT	S1.1	DBP	15.00	0.44
		SBP	17.20	0.44
	S1.2	DBP	14.26	0.49
		SBP	16.96	0.46

Table 2: AAMI Comparison

		Mean Difference (mmHg)	Standard Deviation
AAMI		±5	<8
PAT	DBP	-9.968	10.812
	SBP	-10.029	14.039
dPAT	DBP	-7.722	11.607
	SBP	-9.865	14.443

Discussion

Challenges

Due to COVID-19, the team faced challenges getting IRB-HSR approval and completing the Capstone study. During the IRB-HSR approval process, an additional form was needed to ensure compliance with COVID-19 protocols, and only two researchers would be allowed to collect data in the lab. Additionally, the team determined that their subject pool would decrease from any Charlottesville resident to only University of Virginia staff and students. This was for the researcher's safety, as this subject pool would be undergoing weekly COVID-19 testing, per University guidelines. After the study was granted IRB approval, a second challenge presented itself as the University of Virginia closed laboratories to undergraduate researchers for 2 weeks due to an increase in COVID-19 cases. This delayed the collection of subject data, pushing back the project timeline.

Challenges were also faced with data collection due to mechanical issues with the device. The first challenge was an inability to get the data off of the DEPART device using the external software due to faulty microSD cards. This made the first trial of data unusable for the researchers. The second trial also had mechanical issues due to noisy PPG data. We determined that this was due to light artifacts between the skin and the PPG sensor. We also determined that light artifacts of this magnitude could not be filtered out, and led to a breakdown in the ability of the code to correctly determine the fiducial points on the PPG. To mitigate this issue the finger PPG was readjusted to decrease noise. Due to time limitations, COVID-19, and the technical difficulties with the device, the team was only able to get measurements from two subjects. The measurements from one of these objects was not aligned correctly between the wrist and chest units due to a time delay, so that data was also found to be unusable. The team had hoped to measure blood pressure from 20 subjects, but proceeded with a lesser number due to time constraints.

Additionally, due to time constraints related to data collection, it was determined that machine learning algorithms would take too much time to process. Therefore, regression analysis was employed to determine which metric for blood pressure, PAT or dPAT would be more accurate.

Alternatives

In this project, only the dPAT and PAT were compared using regression analysis. There are a number of other alternatives that would also correlate to blood pressure. The first alternative would be to examine the efficacy of different fiducial points on the PPG. These could include the PPG foot point, or the point on the PPG with the steepest slope.[9] Using different fiducial points could give a more accurate reading if picking each point is more accurate. Specifically, using the PPG foot point would equate to a longer PAT, which could allow for less error in the measurements. Additionally, a PPG could be used on other parts of the body. PPG sensors have been attached to the foot of the subject in other studies.[27] Placing a PPG sensor on the foot could allow for a longer PAT, it could also allow for a larger dPAT measurement. This could lead to less error in data points, and could also be an unobtrusive location for a blood pressure monitor. Additionally, a different measure of pulse transit time (PTT) can be used and compared to PAT. This measurement is defined as the time it takes the pressure wave of a heartbeat to travel between two arterial sites.[12] With the current device, this has been found between the chest and finger PATs waveforms. In other applications, it has been found between the valley point of the arterial blood pressure (ABP) waveform, and a fiducial point on the PPG. This has been shown to be a more accurate correlation to blood pressure due to the absence of a pre-ejaculation period (PEP).[14–16] However, the ABP is found through an invasive method, and thus may not be a feasible measurement for an ambulatory blood pressure monitor.

Another alternative to that proposed in the study would be the use of Machine Learning methods as an alternative to the regression models. This would give a more robust understanding of the parameters included than the regression model used in this project. In past studies, PPG data has been used within neural networks to estimate SBP and DBP signals. This method outperformed linear regression, and thus would be a good alternative to the method used in this project.[12] A more robust Deep Learning algorithm has also been used, which includes a convolutional neural network, a bidirectional gated recurrent unit, and an attention mechanism.[11] Using either of these methods could lead to more accurate DBP and SBP models.

Further Improvements

In the future, this project could be improved by a number of changes. The first would be using more subjects and a wider range of subjects. This is important because the regression analysis could be trained better on a larger amount of data. Additionally, a more diverse subject population would ensure a universal model is created. This is important because of the socioeconomic, and demographic differences in blood pressure.[28,29] By training the model on a number of patients with different baseline blood pressures because of race, age, gender, or economic status, we could ensure that the model is accurate for all patients.

Additionally, it may be helpful to include multiple comparison devices in the study. Throughout the study, there were problems with the Human NIBP Nano system stopping in between measurements. This was due to issues with the finger cuffs inflating properly. Because of these issues, there may be discrepancies within the comparison data. By adding numerous comparison devices, we would be able to ensure that the comparison data is as accurate as possible. One of these devices could be a manual blood pressure cuff, taken at different intervals throughout the

study. Another could be the CareTaker device, which is another FDA approved device that measures continuous "beat-to-beat" blood pressure, heart rate, and other physiological parameters using only a finger cuff.[30]

End Matter

Author Contributions and Notes

K.C., A.D., K.P., and E.R. wrote the paper and designed research protocol, E.R performed data collection and created the PPG, PAT, and PTT data, A.D. performed data collection and created the HRV metrics, K.C. performed data analysis and created the regression models in MATLAB. The authors declare no conflict of interest.

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