Validation of Cuffless Blood Pressure Measurements Using the Perin Health Patch

June 03, 2024

Perin Health Devices

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1.0 Objectives

The primary aim of the study is to validate a proprietary cuffless blood pressure algorithm using measurements from a chest-worn medical device, the Perin Health Patch (PHP). The study will compare the performance of the PHP to an ambulatory blood pressure cuff across 85 subjects for a 20-minute monitoring period and confirm that the wearable device performance meets AAMI standards. The specific objectives are:

- To calculate the mean error and standard deviation of blood pressure (BP) measurements from the PHP relative to the ambulatory blood pressure cuff.
- To determine the compliance of the PHP's mean absolute error (MAE) and standard deviation (SD) with AAMI standards: ≤ 5 mmHg MAE with ≤ 8 mmHg SD for systolic and diastolic BP.

2.0 Background/Rationale

Hypertension, or HBP, is a major modifiable risk factor for cardiovascular diseases (CVDs), which are the leading cause of death globally [1]. Continuous BP measurements are vital for the early prevention, detection, evaluation, and treatment of hypertension and related CVDs due to its prognostic value for BP variability (BPV) [2]. Non-invasive, continuous monitoring at home can enhance patient management by allowing timely therapy adjustments, early detection of cardiac issues, and better management of chronic cardiac conditions, leading to improved patient outcomes and reduced healthcare costs.

Current hypertension guidelines emphasize the importance of out-of-office BP measurements to confirm elevated BP and monitor changes over time. Continuous monitoring of hemodynamic parameters traditionally requires invasive techniques such as arterial lines. These methods are impractical for home use due to the need for specialized equipment and skilled personnel, along with associated risks like infection and thrombosis [3], [4]. Traditional cuff-based home BP devices, which have been the standard for decades, face limitations such as patient adherence, cuff fit, measurement technique, and physical discomfort. Additionally, these devices cycle every 15-30 minutes and cannot reliably capture BP variability and rapid changes, which are crucial for high-risk patients, especially post-operative ones [5].

Recent advances in photoplethysmographic (PPG) sensors have enabled the development of non-invasive and continuous heart rate (HR) and BP monitoring devices. PPG detects blood volume variations in vessels by measuring changes in light absorption. BP is estimated from pulse transit time (PTT), the time taken by the arterial pulse to travel from the heart to a peripheral site. PTT is related to BP through the pulse wave velocity (PWV), which depends on the elastic modulus of the vessel wall, blood density, and arterial dimensions [6]. However, previous systems have failed to meet clinical thresholds set by the British Hypertension Society (BHS) and AAMI, which require a mean estimation error (MAE) of less than 5 mmHg and a standard deviation of less than 8 mmHg [7]. Challenges include inaccurate BP estimations, the need for regular recalibration, and the influence of complex biological processes like vascular tone on measurements [8], [9], [10].

Our study aims to validate a proprietary cuffless BP measurement algorithm using a chest-worn medical device, the Perin Health Patch (PHP). This algorithm leverages the multimodal sensing capabilities of the wearable health patch, which combines noise-immune auscultation, electrocardiography (ECG), pulse oximetry via photoplethysmography (PPG), bioimpedance (BioZ), skin temperature, and motion and tilt sensors. The PHP integrates multiwavelength PPG (MWPPG) with blue, green, red, and IR LEDs, allowing for precise calculation of PTT, PWV, and related unique parameters such as pre-ejection period (PEP) and systemic vascular resistance (SVR). This comprehensive approach aims to improve the accuracy and long-term stability of BP estimations by incorporating biological system knowledge and modeling nonlinear relationships between measured and estimated BP values, consequently improving systolic BP (SBP) and diastolic BP (DBP) estimations.

3.0 Study Design and Procedures

This study will be conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki (2013). Ethics approval will be sought and obtained from the relevant institutional review board before the initiation of the study. All participants will be provided with detailed informed consent forms, ensuring that they fully understand the nature of the study, their rights as participants, and the potential risks and benefits involved. The consent forms will emphasize the voluntary nature of participation, ensuring that participants are free to withdraw from the study at any time without penalty. Additionally, measures will be implemented to protect the privacy and confidentiality of all participants, including the secure handling and storage of data. Throughout the duration of the study, the well-being, autonomy, and dignity of all participants will be upheld and respected.

3.1 Study Design

This is a prospective study designed to validate the PHP by comparing its BP measurements with those from an FDA-cleared ambulatory BP cuff (Norav NBP One) . The study will include 85 participants who will undergo a series of BP measurements over a 20-minute period while simultaneously wearing the PHP and ambulatory BP (ABP) cuff. This study will be conducted in home and office environments, including patients' homes and the offices of Perin Health Devices (21241 Ventura Blvd., Suite 272, Woodland Hills, CA 91364). An initial BP measurement will be taken, followed by four reference BP measurements and three paired test device measurements.

The study will also include an optional cold pressor test to further evaluate the device's performance on intra-patient variability. The cold stimulus activates afferent sensory pathways that, in turn, trigger a sympathetic response resulting in an increase in BP. If a subject elects to participate in the cold pressor test, the validation measurements will be repeated after placing their hand in ice water for one minute.

According to AAMI standards, this study design will ensure the mean absolute error (MAE) between the PHP and the reference device does not exceed 5 mmHg with a standard deviation (SD) of ≤ 8 mmHg for both SBP and DBP.

3.2 Study Type
This study is a Prospective Review: the data do not currently exist and will be collected over the course of this study to conduct the validation.

3.3 Date Range of Data
The study will be conducted from June 15, 2024 to September 15, 2024.

3.4 Study Procedures
The study will be conducted in environments where the PHP is expected to be used, including in participants' homes, office environments, and clinical environments. The study will be conducted in a private environment away from other people. There will be no costs to subjects for participating in the study. Subjects will not be compensated for their participation.

The study will be conducted by the following steps:

1. Participants will be identified through self-selection via an online form shared broadly across social media, email, and web. The online form will include: (1) a description of the study (2) overview of the risks and benefits (3) contact information form. See Appendix E for the online form overview. For participants who elect to participate, they will be contacted by the study team to schedule a time to conduct the study. If the participant is not able to be contacted by phone, a follow-up email will be sent.
2. During the scheduled time, the participant will be provided with an overview of the study, including the study's purpose, procedures, risks, and benefits, and will be given the opportunity to ask questions. The participant will then be asked to sign and complete the consent form. The consent form will be scanned and stored securely in an electronic format for the study team. The physical copy will be returned to the participant.
3. The participant will complete an intake form to gather demographic and medical history information. Information collected will be any exclusion criteria, age, sex, height, weight, ethnicity, history of disease, history of smoking, and history of hyper- or hypotension. On this intake form, the subject will indicate whether they are willing and able to undergo the cold pressor test.
4. For patients with significant chest hair that would occlude the optical measurement, the participant will be asked to shave the region where the device will be placed. The study team member will then measure the skin tone. This skin tone image will be taken against a calibration color palette to normalize all images and an objective skin tone will then be calculated using a detailed representation using a multidimensional measure of apparent skin color [11]. Study team members should be sure that the face is not captured in the skin color photo.
5. The application site will be cleaned using an alcohol wipe and the PHP will be adhered to the participant's chest. The ABP cuff will be placed on the left arm, following the procedure outlined in their instructions for use (IFU).

6. The validation procedure starts with the subject seated comfortably and relaxed for at least 5 minutes, her/his back and arm supported with the middle of the upper arm at heart level, legs uncrossed, and feet flat on the floor. Talking and any other interference will be avoided throughout the entire validation procedure.
7. A timer is started and an initial measurement is taken: a reference BP measurement (R_0) followed by a test device measurement (T_0) to confirm the PHP function. A calibration measurement using a third BP device will be taken when T_0 is taken to calibrate the PHP.
8. Four reference BP measurements follow, alternated by three test device measurements (R_1-T_1-R_2-T_2-R_3-T_3-R_4) (See Table 1). R_x measurements will be performed with 2-minute intervals, with T_x measurements occurring 15 seconds after an R_x measurement. The recordings will be synchronized using absolute time measurements as well as a timer that is started.
9. The participant will optionally undergo the cold pressor test if they indicated on the intake form that they are willing and able to participate. If they opt not to undergo the cold pressor test, skip to Step 10. If they do opt to undergo the cold pressor test, the hand contralateral to the arm with the ambulatory blood pressure cuff will be submerged in ice water ($\leq$ 5 ºC) for at least 1 minute. The study team member will record the temperature of the ice water at the start of the cold pressor test. The participant may opt to remove their hand at any time if they are experiencing high levels of discomfort. After 1 minute the participant will be instructed to remove their hand.
10. Validation measurements from Table 1 will be repeated as soon as the subject removes their hand. Four reference BP measurements follow, alternated by three test device measurements (R_1-T_1-R_2-T_2-R_3-T_3-R_4) (See Table 1). R_x measurements will be performed with 2-minute intervals, with T_x measurements occurring 15 seconds after an R_x measurement.
11. Following the completion of the measurements, the ABP cuff will be removed from the participant. The participant may also be provided with a hand warmer as the following steps are completed.
12. The participant will complete a 5-question survey of Likert-type questions related to comfort and usability of the PHP (See Appendix C).
13. The PHP will then be removed from the participant's chest. The study team members should be sure to use the adhesive remover to minimize any pain or discomfort from the removal of the adhesive.
14. The participant will be discharged from the study and provided with follow-up contact information along with a copy of the consent form.

If the investigator or participant notes an adverse reaction during the testing period, any monitoring devices will be removed immediately, and the subject will be discharged from the study.

Table 1. Procedure for reference and test device BP measurements in sequential validation method.

Initial BP measurements for device function confirmation and calibration		
1.	Take reference BP measurement from BP device.	R_0
2.	Take test device BP measurement, calibration measurement	T_0, C_0
Validation BP measurements for accuracy evaluation		
3.	Take first reference BP measurement	R_1
4.	Take first test device BP measurement	T_1
5.	Take second reference BP measurement	R_2
6.	Take second test device BP measurement	T_2
7.	Take third reference BP measurement	R_3
8.	Take third test device BP measurement	T_3
9.	Take fourth reference BP measurement	R_4

3.5 Process for Data/Specimen Procurement

- Pre-enrollment contact information and screening will be conducted over Google Forms. The information will be collected on a digital spreadsheet. The Google form is shown in Appendix E.
- Data from the ABP cuff will be collected using a PC computer program. The program will output SBP, DBP, and precise measurement time.
- Data from the PHP will be collected using a Bluetooth-enabled tablet. The tablet will provide synchronized 30-second measurements of each measurement modality (PPG, ECG, BioZ, auscultation, motion, skin temperature) sampled at their respective pre-established sampling rates and the precise measurement time.
- The intake form will be provided physically to the participants. Following the data collection, the values from the intake form will be captured in an electronic spreadsheet.
- The consent forms will be scanned and saved in a secure, encrypted folder. The physical copies of the consent forms will be returned to the participant.

3.6 Record Review

N.A., no record review will be conducted as part of this study.

3.7 Database Access

N.A., no access to a pre-existing database will be conducted as part of this study.

3.8 Data/Specimen Storage

Pre-enrollment contact information and screening questions will not be retained/stored after the conclusion of the study.

The patient will be assigned a random ID at enrollment and this random ID will be used to link the intake form, the ABP measurements, and the PHP measurements. No other identifier will be used other than the random ID. The random ID will not be included in the consent form.

Raw data will be securely retained electronically for future secondary analysis. Due to the nature of this data and the use of this data in a regulatory approval, the electronic data

files will be maintained. The data will be stored in a local, encrypted database located at the offices of Perin Health Devices (21241 Ventura Blvd., Suite 272, Woodland Hills, CA 91364). Physical artifacts (completed intake forms) will be stored securely in a locked filing cabinet in a private office at the offices of Perin Health Devices for three years and then destroyed.

Access to the data will be restricted to the study team. If any future or secondary analysis is conducted by other investigators, a formal approval process will be undertaken, including the validation of proper training certificates and data use plans. Training, requests, and approvals will be maintained in Perin Health Devices' electronic quality management system (eQMS). PI McLane will be responsible for the oversight of the electronic and physical data.

4.0 Data/Specimen Analysis

4.1 Data Analysis Plan

Blood pressure from the PHP will be calculated using a proprietary algorithmic approach. The steps include:

1. Preprocessing: Areas of high motion, as determined by the accelerometer measurement are excluded from the analysis. For ECG and PPG signals, artifacts such as baseline wandering and respiratory components at lower frequencies, as well as power line harmonics and electromyogram artifacts at higher frequencies are removed. Auscultation signals are filtered to remove lung sound components and concentrate on heart sound components.
2. Segmentation: Fiducials for the ECG, PPG, and auscultation signals are extracted using respective techniques.
3. Depth-Resolved PPG: The time difference between the capillary component (blue LED) and the arteriolar component (red/IR LED is used to calculate arteriolar PTT and SVR.
4. Feature Extraction: A combination of hand-crafted features and learned feature embeddings are extracted and concatenated into a single feature vector.
5. Deep Learning Estimation: An LSTM-based model is used to estimate SBP and DBP from the calibration value and the input feature vector.

The mean error and standard deviation of the SBP and DBP measurements from the PHP relative to the ambulatory blood pressure cuff will be calculated. Statistical analysis will include paired t-tests and Bland-Altman plots to assess the agreement between the two devices.

The feature extraction and estimation analysis will be conducted by PI McLane, blinded to reference values to maintain data analysis integrity, pursuant of the company's conflict of interest policies. The evaluation and statistical comparisons against the ABP cuff will be conducted by Co-I Rennoll with independent validation by Toon Prasertsit. RN, an independent reviewer. The criteria for validation will follow AAMI standards, where the mean difference must be ≤ 5 mmHg and the standard deviation ≤ 8 mmHg.

4.2 Power Calculation

Based on the AAMI/ESH/ISO consensus standard, a sample size of 85 participants is sufficient to achieve a power of 80% with an alpha level of 0.05 to detect a mean difference in blood pressure measurements between the two devices.

4.3 Data Integrity

A proprietary signal quality index (SQI) will be used to confirm the quality of the signals during recording as well as during post-processing analysis. This SQI will be used to prospectively remove sections of data that may result in poor performance due to motion artifacts or other noise contaminations.

5.0 Eligibility/Subject Enrollment

5.1 Inclusion Criteria

- Adults aged 18 years or older,
- Willing and able to provide informed consent,
- Able to comply with study procedure.

5.2 Exclusion Criteria

- Any member defined under 'Special Population' in the AAMI standards (Pregnant, children, arm circumference > 42 cm),
- Patient with a pacemaker,
- History of reactions to medical adhesives,
- Inability to comply with the study procedure,
- Non-English Speaker.

5.3 Age Range

Adults aged 18 years or older.

6.0 Consent Process & HIPAA Authorization

6.1 Consent Process

Participants will be identified through self-selection via an online form shared broadly across social media, email, and web. The online form will include: (1) a description of the study (2) overview of the risks and benefits (3) contact information form. See Appendix E for the online form overview. For participants who elect to participate, they will be contacted by the study team to schedule a time to conduct the study. If the participant is not able to be contacted by phone, a follow-up email will be sent.

The consent process will take place in a private setting before any study procedures are performed. Participants will be informed, in English, about the study's purpose, procedures, risks, and benefits, and will be given the opportunity to ask questions. Participants will be made aware that there will be no negative impacts if they refuse to participate. Consent will be obtained by either PI McLane or Co-I Rennoll from participants engaging in the study. The participant will be provided with a physical copy of the informed consent documentation and asked to provide a signature. The consent form will be scanned and stored securely in an electronic format for the study team. The

physical copy will be returned to the participant. The study procedure may occur immediately after receiving consent.

6.2 Waiver or Alteration of Consent Process
N/A (no waiver or alteration of consent process requested).

6.3 HIPAA Authorization and Waivers
N/A (No HIPAA Authorization and Waiver is requested as no data are associated with or derived from a healthcare service event, data are not entered into medical records, and no PHI is collected or stored).

7.0 Confidentiality

7.1 Confidentiality
Patient contact information will be stored securely. Digital copies will be encrypted, and access controlled. No physical copies of the information will be allowed. All digital copies of patient contact information will be permanently deleted at the end of the study.

Data will be coded and de-identified at the time of collection to protect participant privacy. No link logs to the above identifying information will be created or retained. Raw data files will be retained securely electronically by randomized ID for future secondary analysis. Physical artifacts (completed intake forms) will be stored securely and separately for three years and then destroyed. Data will not be shared with third parties for any reason other than for formal auditing purposes.

7.2 Data Security
Ensuring data security throughout the study is crucial. Data security measures include:

- Encryption: All data will be encrypted during storage and transmission using strong encryption protocols (e.g., AES-256).
- Access Control: Restricted access to the data to authorized personnel only. Implement multi-factor authentication and role-based access controls for digital data. Physical artifacts will be stored securely in a locked filing cabinet in a private office.
- Regular Audits: Conduct regular security audits to ensure that data protection measures are effective and up to date.
- Training: Provide data security training for all personnel involved in the study to ensure they understand and adhere to data protection protocols. Authorized personnel will be required to complete data handling training prior to receiving authorization of access.

8.0 Risks and Benefits:

8.1 Risks
Risks associated with the study include potential discomfort from BP measurements and the cold pressor test. Additional risks are associated with the adhesive from the PHP, including discomfort when placing or removing the adhesive or an adverse reaction to the

adhesive. There is also a risk of breach of confidentiality, which will be mitigated through secure data handling practices.

The PHP device is not FDA approved. However, we have determined that the device does not introduce any significant risk to the participant and therefore does not require an IDE (i.e., the device is IDE Exempt). See Appendix D for the IDE Exemption justification.

8.2 Benefits

Participants may not receive direct benefits from the study, but the findings could contribute to the development of improved BP monitoring technologies, benefiting society and the field of medical research.

9.0 References

[1] "The top 10 causes of death." Accessed: Dec. 21, 2021. [Online]. Available: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death

[2] G. Parati, J. E. Ochoa, C. Lombardi, and G. Bilo, "Assessment and management of blood-pressure variability," *Nat. Rev. Cardiol.*, vol. 10, no. 3, Art. no. 3, Mar. 2013, doi: 10.1038/nrcardio.2013.1.

[3] R. Klabunde, *Cardiovascular Physiology Concepts*. Lippincott Williams & Wilkins, 2011.

[4] P. Palatini and R. Asmar, "Cuff challenges in blood pressure measurement," *J. Clin. Hypertens.*, vol. 20, no. 7, pp. 1100–1103, 2018, doi: 10.1111/jch.13301.

[5] L. Lonjaret, O. Lairez, V. Minville, and T. Geeraerts, "Optimal perioperative management of arterial blood pressure," *Integr. Blood Press. Control*, vol. 7, pp. 49–59, Sep. 2014, doi: 10.2147/IBPC.S45292.

[6] D. Buxi, J.-M. Redouté, and M. R. Yuce, "A survey on signals and systems in ambulatory blood pressure monitoring using pulse transit time," *Physiol. Meas.*, vol. 36, no. 3, p. R1, Feb. 2015, doi: 10.1088/0967-3334/36/3/R1.

[7] G. S. Stergiou *et al.*, "A Universal Standard for the Validation of Blood Pressure Measuring Devices: Association for the Advancement of Medical Instrumentation/European Society of Hypertension/International Organization for Standardization (AAMI/ESH/ISO) Collaboration Statement," *Hypertension*, vol. 71, no. 3, pp. 368–374, Mar. 2018, doi: 10.1161/HYPERTENSIONAHA.117.10237.

[8] J.-R. Hu *et al.*, "Validating cuffless continuous blood pressure monitoring devices," *Cardiovasc. Digit. Health J.*, vol. 4, no. 1, pp. 9–20, Feb. 2023, doi: 10.1016/j.cvdhj.2023.01.001.

[9] J. Grensemann, "Cardiac Output Monitoring by Pulse Contour Analysis, the Technical Basics of Less-Invasive Techniques," *Front. Med.*, vol. 5, p. 64, Mar. 2018, doi: 10.3389/fmed.2018.00064.

[10] G. M. London and M. E. Safar, "Autonomic nervous system and large conduit arteries," in *The Arterial System in Hypertension*, vol. 144, M. E. Safar and M. F. O'Rourke, Eds., in Developments in Cardiovascular Medicine, vol. 144. , Dordrecht: Springer Netherlands, 1993, pp. 181–194. doi: 10.1007/978-94-011-0900-0_12.

[11] W. Thong, P. Joniak, and A. Xiang, "Beyond Skin Tone: A Multidimensional Measure of Apparent Skin Color." arXiv, Oct. 03, 2023. Accessed: May 13, 2024. [Online]. Available: http://arxiv.org/abs/2309.05148

10.0 Appendices

- Appendix A- Consent Form
- Appendix B- Participant Intake Form
- Appendix C- Device Survey
- Appendix D- IDE Exemption Letter

Appendix A- Consent Form

Consent for Research Participation
Title: **Validation of Cuffless Blood Pressure Measurements Using the Perin Health Patch** Investigator/Researcher(s): **Ian McLane, Ph.D.; Valerie Rennoll, Ph.D.** Investigator/Researcher Contact Information: **+1 (818) 606-9389, imclane@phasemargin.com** Sponsor: **Phase Margin, Inc.**

KEY INFORMATION FOR YOU TO CONSIDER

We (the researchers) are asking if you would like to be in a research study. Some key information is provided in the boxes below to help you decide if you want to participate or not. Read the entire form and ask questions before you decide. The researchers will go over this form with you and you can ask any questions.

What is the purpose of this research?	The purpose of this research is to see if a new chest-worn medical device called the Perin Health Patch (PHP) can measure blood pressure accurately without using a traditional arm cuff. We want to compare the PHP's measurements to those from a regular blood pressure cuff to make sure it meets the standards for accuracy. The PHP is not FDA-approved, but the results from this research will be used for a future FDA submission and approval.
What will happen to you during the study?	During the study, you will fill out an intake form with information like your age, sex, height, ethnicity, and medical history. If you have a significant amount of chest hair, we will ask that you shave the device placement area. We will place the Perin Health Patch (PHP) on your chest and take a calibration measurement followed by four blood pressure measurements using both the PHP and a regular blood pressure cuff, with a 2-minute break between each measurement. If you agree, you will put your hand in ice water for 1 minute as part of a cold pressor test and then repeat the four blood pressure measurements. Finally, you will complete a short survey about the comfort and usability of the PHP before we remove the PHP from your chest, and you will be done with the study.
How long will you be in the research?	You will be in the research study for about 10 minutes for the initial measurements. If you choose to do the cold pressor test, it will take an additional 10 minutes. So, the total time you might spend in the study may be about 20 minutes.
Could being in this research harm you?	You should understand the risks of this research study before you decide to participate.

	If you participate in this study, you might experience some minor risks and discomforts that might include the following: • Wearing the Perin Health Patch (PHP) on your chest might feel a bit uncomfortable. • You may have a reaction to the adhesive from the PHP. • The regular blood pressure cuff might cause slight discomfort when it inflates. • If you do the cold pressor test, putting your hand in ice water for 1 minute might feel very cold and uncomfortable. This research is no more than minimal risk. The level of risk is about the same as risks of daily life or a physical exam.
Will being in this study help you in any way?	You will not benefit directly from being in this study. However, the information we learn from the study could help develop better ways to measure blood pressure without using a traditional cuff, which might benefit other people in the future.
Are there any costs to participate?	It does not cost anything to be in the study.
How do researchers protect your information?	Researchers keep your personal information confidential and stored securely. Only the researchers approved to be on this study may see your information.
Will you get any test results?	The results of research tests are not given to you. Results of research tests have no clear meaning for your health care.

ADDITIONAL DETAILED INFORMATION

What will happen to you if you decide to be in the study?

1. You will complete an intake form to gather demographic and medical history information. On this intake form, you will indicate if you are willing and able to undergo the cold pressor test.
2. You may be asked to shave the region where the device will be placed. The study team members will then measure the skin tone where the PHP will be placed.
3. The application site will be cleaned using an alcohol wipe and the PHP will be adhered to your chest.
4. You will be asked to stay seated comfortably and relaxed for at least 5 minutes, with your back and arm supported with the middle of the upper arm at heart level, legs uncrossed, and feet flat on the floor. Talking will be avoided throughout the entire process.
5. Blood pressure measurements from the blood pressure cuff and the PHP will be taken several times over the course of 10 minutes.

6. If you indicated on the intake form that you are willing and able to participate in the cold pressor test, the hand opposite the arm with the cuff will be placed in ice water for at least 1 minute. You can remove your hand at any time if you are very uncomfortable. After 1 minute, the study team member will tell you to remove your hand.
7. Blood pressure measurements from the blood pressure cuff and the PHP will be taken again several times over the course of 10 minutes.
8. The cuff will be removed after the last measurement.
9. You will be asked to complete a 5-question survey of Likert-type questions related to comfort and usability of the PHP.
10. The PHP will then be removed from your chest and you will be done with the study.

Could being in this research harm you? (Detailed Risks)

You may experience discomfort from the blood pressure cuff when inflating.

You may experience skin irritation from the PHP adhesive.

You may experience some pain or discomfort when removing the PHP from your chest.

You may experience some discomfort when placing your hand in the ice water for the cold pressor test.

Please let the study team member know if at any moment you feel discomfort. It is okay if you wish to discontinue your participation at any time.

There may be unknown risks in this research. Tell the researchers if you develop a new condition or injury.

Is there any available medical treatment or compensation if injured in the study?

This study is no greater than minimal risk, so no medical treatment or compensation will be available.

How many people will participate in this research study?

The researchers hope to enroll up to 85 people.

Who can you talk to about the research?

Contact the researcher listed on the first page if you have questions, concerns, complaints, or get hurt.
Pearl Institutional Review Board (IRB) oversees this research. You may call (317) 899-9341 to speak to the IRB for any reason, such as:

- You have questions about your rights.
- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You want to get more information.

- You want to provide your input about this research.

Will the researchers return results and incidental findings to you?

In general, we will not give you any individual results from the study of the samples you give us. If we find something of urgent medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

Are there any conflicts of interests reported for this study?

Dr. McLane is an officer of the sponsor institution, Perin Health Devices, but does not contain any financial ownership in Perin Health Devices. The outcome of this research study could be of interest to Perin Health Devices. The IRB oversees the conflict of interest policies. In accordance with these policies, the IRB has determined that Dr. McLane's interests create no significant risk to the welfare of participants in this study or to the integrity of the research. If you want more information about this, please contact the IRB.

How do researchers protect your information?

The researchers will keep information about you in a secure location with limited access. If the results of this study are made public, information that identifies you will not be used.

What Protected Health Information will be used or disclosed?

Federal law protects your right to privacy concerning PHI. There are certain things you need to know. PHI is any information from your medical record or obtained from the study linked to you and that refers to your mental or health conditions in the past, the present or the future. No PHI will be collected in relation to this study.

What information about this study is available to the public?

A description of this clinical study will be available on http://www.ClinicalTrials.gov. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Can your participation end early?

You may end your participation in this study at any time by communicating with the investigator. There will be no consequences if you choose to withdraw from the study.

The investigator may terminate a subject's participation without regard to the subject's consent for any of the following reasons:

- If you are a female who becomes pregnant
- If the research becomes harmful
- If you do not follow the instructions or adhere to the research requirements given to you by the study doctor or study staff

- You do not take medication as instructed
- You do not keep study appointments

Will you receive anything for being in the research?

You will NOT receive any gifts, rewards, compensation, or reimbursement for your participation in this research study.

May the researchers share your coded information for future research? • The researchers approved for this current study will deidentify your materials immediately. • The researchers doing future research with the deidentified materials cannot identify you. • The following materials may be used in future research: raw recordings from the PHP, blood pressure measurements from the cuff, information from the intake form. • Future research may include time series analysis of ECG, PPG, auscultation, BioZ, motion, or temperature; refinement of blood pressure estimation algorithms. • Your deidentified information will be maintained for as long as it is useful for research purposes, after which time the specimen and information will be destroyed. • You will not be able to get individual research results about you because the researchers who receive your materials will not have your identifiers.	
Please initial the ONE option that you choose below:	
_____ *(initials)*	YES. *You still have the right to withdraw this authorization later.*
_____ *(initials)*	NO.

SIGNATURES

You have read this document and were told of the risks and benefits and a member of the research team answered questions to your satisfaction. A member of the research team will answer any future questions. You voluntarily agree to join the study and know that you can withdraw from the study at any time without penalty. You do not waive any legal rights by signing this form.

You will receive a signed copy of this document.

_____ **Print the Name of the Adult Research Participant** (18 years of age or older)	_____ **Signature of the Adult Research Participant**	_____ **Date Signed**
Completed by the Investigator obtaining informed consent: ☐ In addition to advising the person authorizing the research about any appropriate alternatives to research participation, I have offered an opportunity for further explanation of the risks and discomforts which are, or may be, associated with this research, and to answer any further questions.		

☐ Check to confirm participant agreed to participate in the study and signed the informed consent form(s) and all questions were answered. *Check options pertaining to remote consent if applicable:* ☐ Check if remote consent (conference call or video conference). ☐ Check if the informed consent document was not retained, due to contamination of the document by infectious material. ☐ Check to confirm participant was asked to mail, fax, or e-mail a copy of the signed consent to the research team.		
_____ **Print Name of Investigator Obtaining Informed Consent**	_____ **Signature of Investigator Obtaining Informed Consent**	_____ **Date Signed**

Appendix B- Participant Intake Form

PATIENT ID: _____

AGE: _____ ☐ Over 90 or older

DO ANY OF THE FOLLOWING APPLY TO YOU?

I am pregnant. ☐ YES
I have a pacemaker. ☐ NO
I have previously had a reaction to adhesives.
I cannot complete this study for other reasons.

----------If you answered yes to the above question, please stop and inform the study team member.----------

BIOLOGICAL SEX: ☐ Male ☐ Female

HEIGHT: _____ ft _____ in **WEIGHT:** _____ lbs

ETHNICITY:
(Check all that apply)

☐ American Indian or Alaska Native
☐ Asian
☐ Black or African American
☐ Hispanic or Latino
☐ Native Hawaiian or Other Pacific Islander
☐ White (non-Hispanic)
☐ Other

HISTORY OF HYPERTENSION (High Blood Pressure): ☐ Yes ☐ No

HISTORY OF HYPOTENSION
(Low Blood Pressure): ☐ Yes ☐ No

ARE YOU ON ANY BLOOD PRESSURE MEDICINE OR BLOOD THINNERS?

☐ Yes ☐ No

HISTORY OF DISEASE:
(Check all that apply)

☐ Coronary artery disease
☐ Congestive heart failure
☐ Arrhythmias (e.g., atrial fibrillation)
☐ Other cardiovascular disease
☐ Chronic obstructive pulmonary disease (COPD)
☐ Asthma
☐ Diabetes mellitus
☐ Peripheral artery disease
☐ Chronic kidney disease
☐ Other: _____

HISTORY OF SMOKING: ☐ Yes ☐ No

ARE YOU WILLING AND ABLE TO UNDERGO THE COLD PRESSOR TEST?

☐ Yes ☐ No

Appendix C- Device Survey

PATIENT ID: _____

Please rate your level of agreement with the following statements:

1. **I found that the patch was noticeable when wearing it.**

☐ Totally disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Totally agree

2. **I found the patch irritating on my skin.**

☐ Totally disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Totally agree

3. **I found that wearing the patch was painful.**

☐ Totally disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Totally agree

4. **I prefer the patch to the blood pressure cuff for monitoring my blood pressure.**

☐ Totally disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Totally agree

5. **I would wear the patch continuously for one month to help manage my care.**

☐ Totally disagree ☐ Disagree ☐ Neutral ☐ Agree ☐ Totally agree

Appendix D- IDE Exemption Letter

Study Title: Validation of Cuffless Blood Pressure Measurements Using the Perin Health Patch

Study Devices: Perin Health Patch

Sponsor Justification of Non-Significant Risk Device:

The Perin Health Patch in conjunction with its labeling, device classification and indications for use, does NOT meet any of the four criteria set out by the FDA to define a significant risk device. For these reasons, the Perin Health Patch is considered a non-significant risk (NSR) device and is therefore exempt from Investigational Device submissions and FDA oversight.

Definition of a Significant Risk (SR) device under 21 CFR Part 812.3.:

The study device(s) as listed above:

- Is not intended as an implant which would thereby present potential for serious risk to the health, safety, or welfare of a subject;
- Is not purported or represented to be for use in supporting or sustaining human life which would thereby present potential for serious risk to the health, safety, or welfare of a subject;
- Is not used for use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health which would thereby present potential for serious risk to the health, safety, or welfare of a subject; and
- Does not otherwise present potential for serious risk to the health, safety, or welfare of a subject.

Non-Significant Risk (NSR)

- Non-Significant Risk devices are investigational devices that do not pose a significant risk to the human subjects and do not meet the definition of a SR device.

Sponsors of studies involving non-significant risk devices are not required to submit an IDE application to the FDA for approval. Submissions for non-significant device investigations are made directly to the IRB of each participating institution. The FDA considers an investigation of a non-significant risk device to have an approved IDE when the IRB concurs with the non-significant risk determination and approves the study.

The sponsor must comply with the abbreviated IDE requirements under 21 CFR 812.2(b):

- Labeling - The device must be labeled in accordance with the labeling provisions of the IDE regulations (812.5) and must bear the statement "CAUTION - Investigational Device. Limited by Federal (or United States) law to investigational use."
- IRB Approval – The sponsor must obtain and maintain Investigational Review Board (IRB) approval throughout the investigation as a non-significant risk device study (812.2 (b)).

- Informed Consent – The sponsor must assure that investigators obtain and document informed consent from each subject according to 21 CFR 50, Protection of Human Subjects, unless documentation is waived by an IRB in accordance with 56.109(c).
- Monitoring - All investigations must be properly monitored to protect the human subjects and assure compliance with approved protocols (812.46).
- Records and Reports - Sponsors are required to maintain specific records (812.140(b) (4) and (5) and make certain reports as required by the IDE regulations 812.150(b) (1), (2), (3), (5), (6), (7), (8), (9) and (10).
- Investigator Records and Reports – The sponsor must assure that participating investigators maintain records (812.140(a)(3)(i) and make reports as required (812.150(a) (1), (2), (5) and (7); and
- Prohibitions –Commercialization, promotion, test marketing, misrepresentation of an investigational device, and prolongation of the study are prohibited (812.7).

The Perin Health Patch thus has No Major Risks Anticipated.

The Perin Health Patch is a chest-worn device measuring 65 x 35 mm. The device records several vital signs, including skin temperature, electrocardiogram (ECG), pulse oximetry, and heart and lung auscultation. The device is powered from a lithium manganese oxide battery for 16 days of continuous use in a home environment. The electronics module is adhered to the chest with a certified long-term wear adhesive for up to 28 days of wear time.

Perin Health believes it has adequately mitigated anticipated risks through the process outlined in ISO 14971, a nine-part standard which first establishes a framework for risk analysis, evaluation, control, and review for medical devices.

Please feel free to reach out with any further questions regarding the Perin Health Patch or the IDE Exemption and Study Risk Determination.

Ian McLane, Ph.D.

Chief Technology Officer

Perin Health Devices

+1 (818) 606-9389

Appendix E- Pre-enrollment Post Copy & Form

Copy:

Help validate a new cuffless blood pressure monitoring device! Please complete this pre-enrollment survey to learn more about the study, see if you qualify, and to express interest in participating: [survey link].

Pre-enrollment: Validation of Cuffless Blood Pressure Measurements Using the Perin Health Patch

This form will determine your interest in a study to validate cuffless blood pressure measurements using the Perin Health Patch. Participation in this study is voluntary. Even if you decide to join now, you can change your mind later.

Research summary: This study will determine if a new chest-worn medical device called the Perin Health Patch (PHP) can measure blood pressure accurately without using a traditional arm cuff.

- We want to compare the PHP's measurements to those from a regular blood pressure cuff to make sure it meets the standards for accuracy.
- The PHP is not FDA-approved, but the results from this research will be used for a future FDA submission and approval.

Study format:
During the study, the following steps will be completed.

1. You will fill out an intake form with information like your age, sex, height, ethnicity, and medical history.
2. If you have a significant amount of chest hair, we will ask that you shave the device placement area.
3. A study team member will place the Perin Health Patch (PHP) on your chest and take a calibration measurement followed by four blood pressure measurements using both the PHP and a regular blood pressure cuff, with a 2-minute break between each measurement.
4. If you agree, you will put your hand in ice water for 1 minute as part of a cold pressor test and then repeat the four blood pressure measurements.
5. You will complete a short survey about the comfort and usability of the PHP before we remove the device from your chest, and you will be done with the study.

You will be in the research study for about 10 minutes for the initial measurements. If you choose to do the cold pressor test, it will take an additional 10 minutes. So, the total time you might spend in the study may be about 20 minutes.

Risks & benefits:
If you participate in this study, you might experience some minor risks and discomforts that could include the following:

- Wearing the Perin Health Patch (PHP) on your chest might feel a bit uncomfortable.
- You may have a reaction to the adhesive from the PHP.
- The regular blood pressure cuff might cause slight discomfort when it inflates.
- If you do the cold pressor test, putting your hand in ice water for 1 minute might feel very cold and uncomfortable.

This research is no more than minimal risk. The level of risk is about the same as risks of daily life or a physical exam.

Participants may not receive direct benefits from the study, but the findings could contribute to the development of improved BP monitoring technologies, benefiting society and the field of medical research.

vrennoll@phasemargin.com Switch account
Not shared

Next Page 1 of 3 Clear form

Never submit passwords through Google Forms.

This form was created inside of Phase Margin, Inc. Report Abuse

Google Forms

Figure 1. Page 1 of the pre-enrollment form, which provides an overview of the study and its risks and benefits.

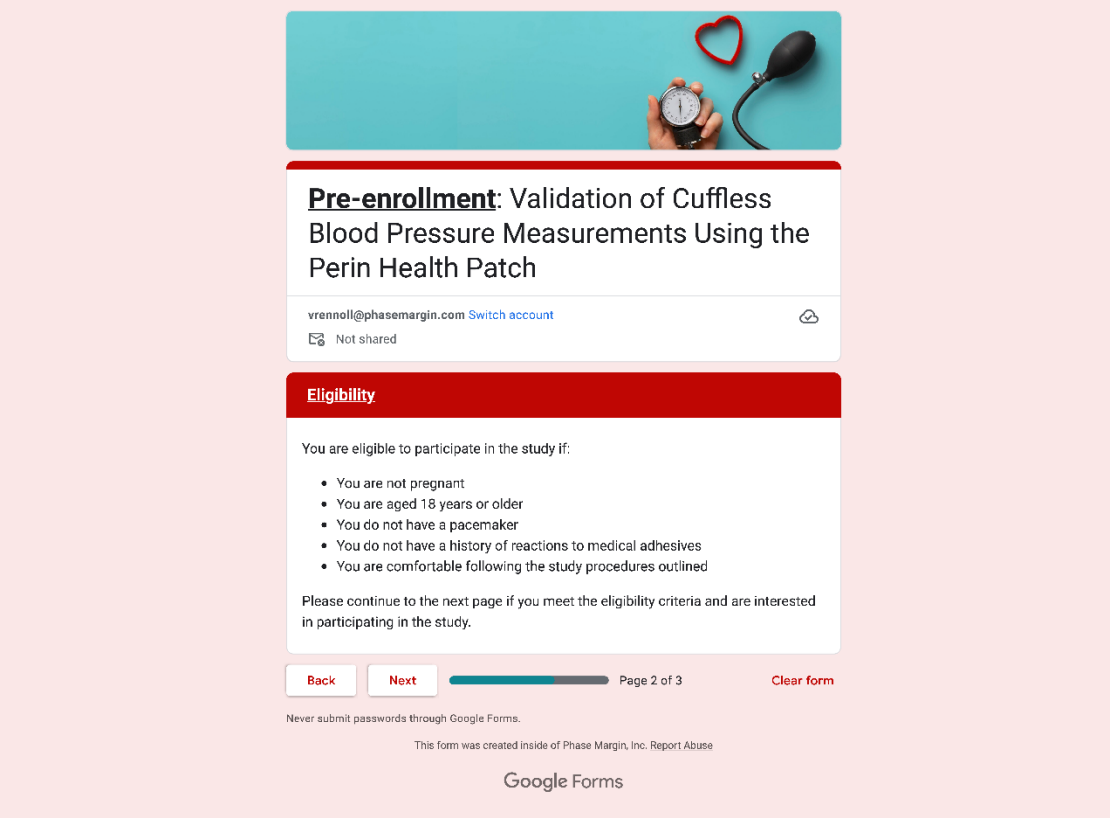

Figure 2. Page 2 of the pre-enrollment form, which outlines the eligibility criteria for the study.

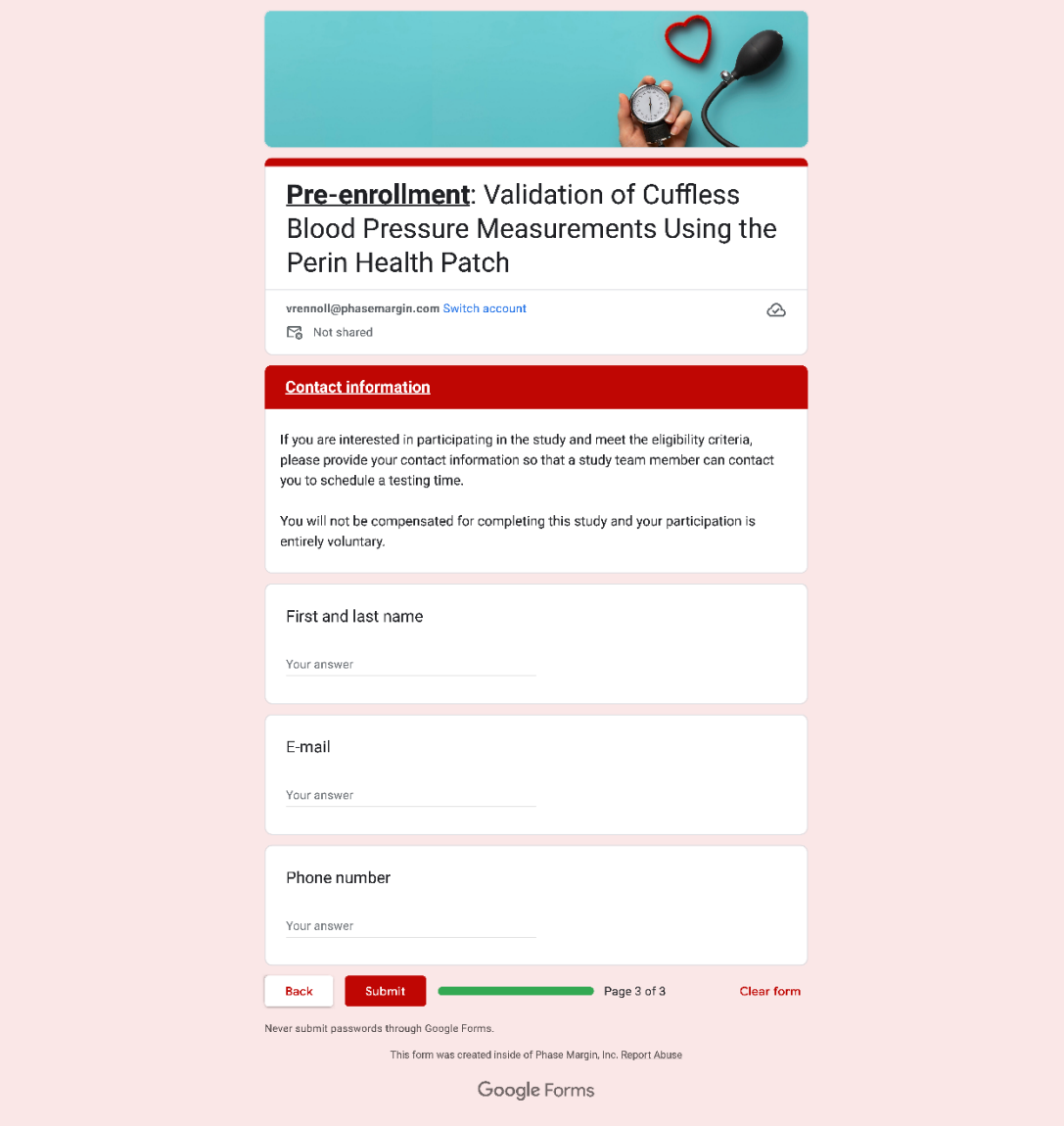

Figure 3. Page 3 of the pre-enrollment form, which collects contact information from subjects, including their name, e-mail, and phone number

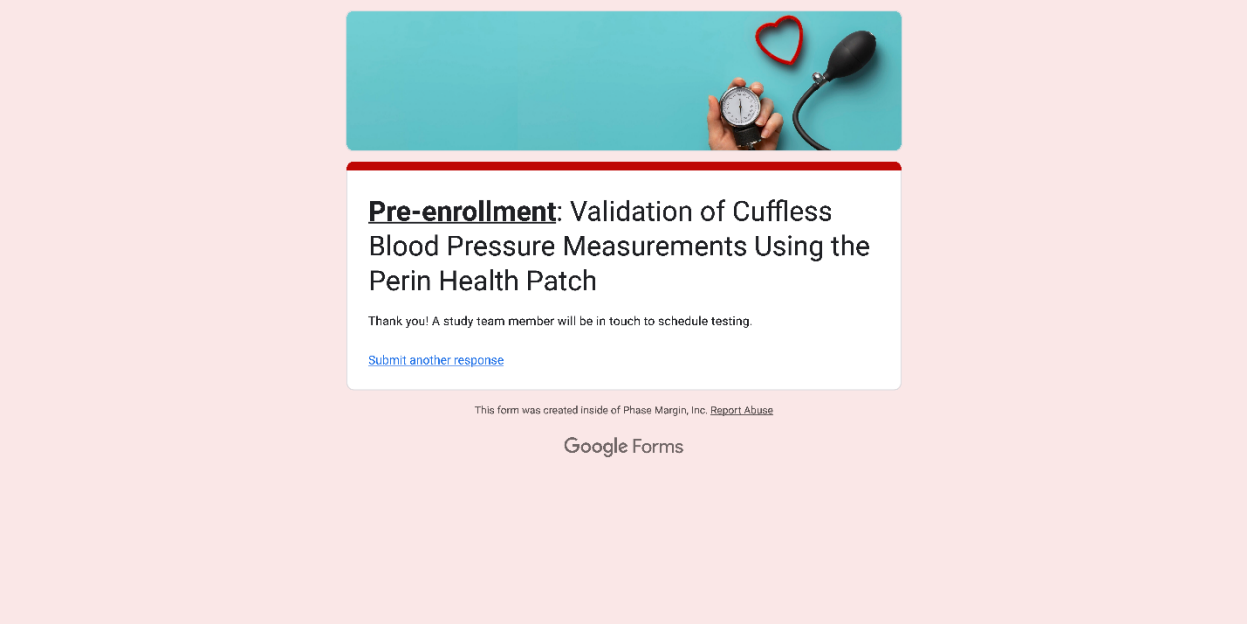

Figure 4. Page 4 of the pre-enrollment form which thanks subjects for their participation.